Departement für Pferde, Abteilung für Anästhesiologie
Vetsuisse-Fakultät Universität Zürich

Direktor: Prof. Dr. med. vet. Anton Fürst

Arbeit unter Leitung von Prof. Dr. med. vet. PhD Regula Bettschart-Wolfensberger

Racemic ketamine in comparison to S-ketamine in combination with azaperone and butorphanol for castration of pigs

Inaugural Dissertation

zur Erlangung der Doktorwürde der
Vetsuisse-Fakultät Universität Zürich

vorgelegt von

Stephanie Rebecca Stauffer

Tierärztin
von Hallwil AG

genehmigt auf Antrag von

Prof. Dr. med. vet. PhD Regula Bettschart-Wolfensberger, Referentin

Prof. Dr. med. vet. Michael Hässig, Korreferent

Zürich, 2012

Vetsuisse-Fakultät Universität Zürich

Direktor: Prof. Dr. med. vet. Anton Fürst

Arbeit unter Leitung von Prof. Dr. med. vet. PhD Regula Bettschart-Wolfensberger

Racemic ketamine in comparison to S-ketamine in combination with azaperone and butorphanol for castration of pigs

Inaugural Dissertation

zur Erlangung der Doktorwürde der
Vetsuisse-Fakultät Universität Zürich

vorgelegt von

Stephanie Rebecca Stauffer

Tierärztin
von Hallwil AG

genehmigt auf Antrag von

Prof. Dr. med. vet. PhD Regula Bettschart-Wolfensberger, Referentin

Prof. Dr. med. vet. Michael Hässig, Korreferent

Zürich, 2012

Table of contents

1. Summaries

1.1 Zusammenfassung

Die vorliegende Studie war ein prospektiver, verblindeter, randomisierter Versuch mit 28 neun Wochen alten Mastschweinen mit einem geschätzten Körpergewicht von 25kg. Die Tiere wurden zur Kastration anästhesiert und erhielten eine intramuskuläre Injektion mit entweder 15mg/kg Ketamin Racemat (Keta-Race) oder 9 mg/kg S-Ketamin (S-Keta) zusammen mit 5 mg/kg Azaperon, 0.2 mg/kg Butorphanol und 0.4 mg/kg Meloxicam. Die Anästhesie Einleitungs-, Kastrations- und Aufwachphasen wurden gescort und die Zeiten gemessen. Bei ungenügender Anästhesietiefe wurde ¼ des initialen Ketamins nachgespritzt.
Die gemessenen Zeiten der Gruppen wurden mit dem T-Test und ANOVA analysiert. Nachdosierungen wurden mit dem Chi-Quadrat getestet und die Scorings mit dem two sample wilcoxon rank-sum test analysiert.
Alle Kastraten überlebten Anästhesie und Operation. Intravenöse Nachdosierung von ¼ des initialen Ketamins war bei 23 Tieren in 46 Fällen nötig und gleichmässig auf beide Gruppen verteilt. Während der Aufwachphase zeigten S-Keta Schweine früher 1. Bewegungen, 1. Sternallage und die Fähigkeit zu Stehen. Drei Kastraten aus beiden Gruppen zeigten Muskelzuckungen. Ein stürmisches Aufwachen mit extensivem Rudern der Gliedmassen wurde bei zwei Tieren der Keta-Race Gruppe beobachtet.
Zusammenfassend führte S-Ketamin in einer Dosierung von 60% vom R/S-Ketamin zu einer vergleichbaren Anästhesie wie Keta-Race. Keines der S-Keta Tiere zeigte eine inakzeptable Aufwachqualität.

Keywords: Kastration, S-Ketamin, Schwein, Anästhesie

1.2 Summary

The present study was a prospective blinded randomised trial with 28 male 9-week-old fatteners with an estimated bodyweight of 25 kg. The pigs were injected intramuscularly either with 15 mg/kg racemic ketamine (Keta-Race) or 9 mg/kg S-ketamine (S-Keta) together with 5 mg/kg azaperone, 0.2 mg/kg butorphanol and 0.4 mg/kg meloxicam to be anaesthetized for castration. Induction, maintenance and recovery from anaesthesia were timed and scored. Anaesthesia insufficient for surgery was deepened by injecting ¼ the initial dose of ketamine into an ear vein.

To analyse the timings for S-Keta and Keta-Race a T-test and for repeated recovery time data ANOVA was used. Concerning re-doses a chi square test was used and the scoring was analysed by two sample wilcoxon rank-sum test.

Every pig survived anaesthesia and was successfully castrated. Additional intravenous ketamine re-dosing was required in 23 animals on a total of 46 occasions distributed evenly throughout both groups. Timings and scorings were different in the recovery phase. The pigs of the S-Keta group showed earlier 1st movements, 1st sternal recumbency and ability to stand. Three fatteners in each group showed muscle fasciculations and two animals of the Keta-Race group showed a rough recovery with extensive rowing and paddling.

In conclusion S-ketamine at a dose rate of 60% of the racemic ketamine induced comparable anaesthesia. None of the pigs with S-Keta showed an inacceptable recovery quality.

Keywords: castration, S-ketamine, anaesthesia, pig

2. Introduction

Anaesthesia in pigs is challenge, especially because of the lack of medications available for this purpose. The only injectable anaesthetic agent licensed for pigs is ketamine. Isoflurane is registered for inhalation anaesthesia in pigs. Due to the necessity of having an inhalation anaesthesia machine, its use under field conditions is difficult. Correct handling of the machine and especially appropriate outlet of the waste gas is essential (Kupper 2008; SUVA 2009). Also does isoflurane cause depletion of the ozone layer and it should only be used if no alternative is available. Furthermore, unconsciousness with isoflurane alone is very short and nociception is not prevented. If no additional pain relief is added, postoperative suffering is considerable.
Ketamine provides some analgesic and is a simple alternative to inhalation anaesthesia in pigs, because it can be injected intramuscularly. Respiration and cardiovascular function are only minimally depressed, but animals may show distressed and excited recoveries (Ganter et al. 1990; Boschert et al. 1996). Therefore ketamine should only be used in combination with sedatives, such as alpha$_2$-agonists or azaperone. As azaperone is the only sedative registered for pigs, its use is first choice. For additional pain it should be used in combination with butorphanol or local anaesthesia, because azaperone is not analgesic (Cornick-Seahorn 2001; Plumb 2002).
Since January 2010 anaesthesia is mandatory for castrating piglets in Switzerland. Although there would be other methods available, each year more than 1.3 million male piglets are castrated in Switzerland to produce boar taint free meat. The most common method to anaesthetize these pigs is the use of inhalation anaesthesia in combination with an intramuscular application of a NSAID (non steroidal anti-inflammatory drugs) for pain relief. Castration is carried out by the farmer. After having participated a state official course, the farmers are allowed to perform inhalation anaesthesia. This practice markedly causes environmental damage, because isoflurane waste gas is evacuated into the atmosphere.

A practical, simple and safe alternative anaesthesia would be injection anaesthesia with ketamine in combination with azaperone and butorphanol. In the past, anaesthesia with ketamine combinations in piglets showed higher death rates, probably due to the higher doses of ketamine used (McGlone & Hellman 1988; Lahrmann et al. 2005), and prolonged and uncontrollable recoveries were observed (McGlone & Hellman 1988).

S-ketamine, which has only become available recently, induced less seizures and better, shorter recovery phases in humans, horses, dogs, cats and syrian hamsters. In these species it was shown to produce equipotent anaesthesia at 50-60% of the racemic ketamine. In pigs there are no data about the use of S-ketamine for surgical anaesthesia available.

2.1 Aim of the study and hypothesis

The aim of the study was to see whether anaesthesia in pigs using S-ketamine (Keta-S® ad us. vet., solution for injection, Dr. E. Graeub AG, Berne, Switzerland) is equal to racemic ketamine (Ketasol® – 100 ad us. vet., solution for injection, Dr. E. Graeub, Berne, Switzerland) in a dosage of 60% of the latter. Furthermore, the hypothesis was that with S-ketamine the recovery phase after general anaesthesia is shorter and quieter.

This study aimed at testing S-ketamine for injection anaesthesia for pig castration in comparison to racemic ketamine. We tested if the intramuscular anaesthesia with S-ketamine at a 60% dose of the racemic ketamine in combination with azaperone and butorphanol produced equal anaesthesia and analgesia, and if recovery was shorter and of better quality.

3. Literature

3.1 Situation of piglet castration in Switzerland

Male piglet castration has a long tradition in Switzerland and around 1.3 million animals get castrated every year (Kupper et al. 2008).
To ensure the sensory meat quality, most male piglets are castrated. The reason being, that in the fattening period of entire, uncastrated males, the boar taint can occur which is an unpleasant odour and flavour mostly attributable to the presence of androstenone and skatole in the meat and fat (Bonneau et al. 1992; Heid & Hamm 2009). Another advantage of castrated pigs is less aggression between fatteners or grown up males and therefore, less injury due to reduced jumping up. Till 2010 most piglets were castrated without anaesthesia and analgesia. Through more criticism on this procedure, especially because there is no evidence that young piglets should feel less pain compared to older pigs, political consequences followed (McGlone & Hellman 1988; McGlone 1993; Heid & Hamm 2009).

3.2 Law principles in Switzerland

Since 1st January 2010 every piglet has to be anaesthetized for castration by federal law (Art. 16 TSchG). The castration has to be performed as gentle as possible (Art. 4 Abs 2. TSchG). Farmers are allowed to castrate their own piglets to the age of two weeks. Therefore, they have to gain a diploma having visited a specific course for anaesthesia. To anaesthetize the piglets the veterinary pharmaceutical drugs need to be licensed. At the moment farmers anaesthetize their piglets by gas inhalation with isoflurane (Isoflo® or Attane®) and for postoperative pain relief there are several NSAIDs registered (Metacam®, Tolfedin® or Finadyne®) from the Federal Office of Veterinary, Information for animal welfare, December 2009 (BVET 2009).

3.3 Non-surgical methods of piglet castration

3.3.1 Boar fattening

Limitations with raising entire males are mainly linked to pork quality and to welfare issues. The most important factor is the higher incidence of boar taint, especially in countries where pigs are slaughtered at medium or high weights. In Great Britain and Ireland pigs get slaughtered at low weight and before sexual maturity, where the boar taint problem is therefore less perceived. Furthermore, entire males may show more aggressiveness and sexual activities than castrates, which may result in carcass damage or skin lesions followed by financial loss for the farmer. Improvement of animal welfare is achieved by experiencing no pain and discomfort of castration. Advantages in raising entire males are superior growth rate of boars, a better feed conversion ratio and therefore less feed intake, leaner carcasses and time effectiveness due to abandoning castration (de Roest et al. 2009; Fredriksen 2009; von Borell et al. 2009). A Swiss project called

ProSchwein detected 4% boar taint in low weight slaughtered boars and 16% in high weight boars with the cooking method. The aim for the future would be to reduce the percentage of boar taint in entire males through genetic selection (Kupper et al. 2008). Consumer reaction towards boar meat is essential. A study concludes that the assumed negative reaction to boar meat of consumers cannot be proven (Heid & Hamm 2009).

3.3.2 Immunovaccination

The sole licensed product for immunovaccination is Improvac® (Pfizer) a gonadotropin-releasing factor hormone analogon (GnRH). The vaccination suppresses testicle function of the vaccinated temporarily. The immunisation regimen comprises two subcutaneous injections in the neck, at least 4 weeks apart. While the first vaccination only primes the pigs immune system, the second one administered 4 to 5 weeks before slaughter stimulates high levels of GnRH antibodies, that neutralise the natural GnRH in the pig, inhibiting testicular function and therefore production of testosterone and androstenone (von Borell et al. 2009). In Australia this technique has been widely adopted since 1998 (de Roest et al. 2009; Fredriksen 2009).
Difficulties with this method are the time-consuming part of injecting each animal twice and costs related to screening on slaughter line (Prunier et al. 2006; de Roest et al. 2009). Customer acceptance for vaccination is low when poorly informed. Accurate and extensive information will be a key solution for marketing this method (Kupper et al. 2008; Heid & Hamm 2009). Advantages of immunocastration by means of Improvac® are higher growth rate and better feed efficiency and leaner meat compared to castrates. Vaccinated animals are less aggressive and show reduced sexual behaviour than entire males (Prunier et al. 2006; de Roest et al. 2009; von Borell et al. 2009; Baumgartner et al. 2010).

3.3.3 Spermasexing

Sperm sexing of boar semen would offer the opportunity to produce only female pigs that would not need to undergo painful surgical castration. This method is not yet found to be practical due to the long time of about 20 hours to isolate one single dose of sexed sperms (von Borell et al. 2009).

3.4 Surgical castration with different anaesthetic methods

3.4.1 General anaesthesia in pigs

General anaesthesia is accomplished by inhalation anaesthesia or by intravenous or intramuscular injection of anaesthetics or combinations of those with other analgesic, sedative or muscle relaxing drugs (Heinonen et al. 2009).
Pigs are considered to be difficult animals to restrain for diagnostic or therapeutic purposes (Nishimura et al. 1993; Boschert et al. 1996; Heinonen et al. 2009). Even for minor surgical procedures, pigs require to be adequately anaesthetized. Surgery under field conditions depends on anaesthetic agents, which can be easily administered.

3.4.2 Inhalation anaesthesia

Gaseous anaesthetics, such as isoflurane, halothane and carbon dioxide (CO_2), have been tested in pigs. Inhalation anaesthesia results in quick anaesthesia induction and fast recovery.

3.4.2.1 Carbon dioxide (CO_2)

In several studies carbon dioxide (CO_2) was studied as an anaesthetic agent (Lauer et al. 1994; Körtel 1996; Kohler et al. 1998). Unwanted side effects include hyperventilation and agitation during induction and gasping during castration.

In a study they identified a most promising CO_2/O_2 mixture for castrating young piglets. With a mixture of 70% CO_2 + 30% O_2 all piglets lost consciousness after approximately 30s according to the EEG. None of the animals showed any reaction to castration in behaviour or on the EEG and ECG. The piglets recovered on average in 59s. To establish maximum time survival, five piglets were put into a chamber of 70% CO_2 + 30%O_2 for 3 minutes. Two of them died (Gerritzen et al. 2008). Obviously there are limitations of safety in terms of concentration and duration of exposure for CO_2 and the Association of Veterinary Anaesthesia and Analgesia (AVA) has expressed great concerns against this method of anaesthesia.

3.4.2.2 Halothane

Halothane as anaesthetic agent was withdrawn from the European market, because of dangerous pollution of the environment, and is therefore no alternative for anaesthetizing piglets for castration any more.

3.4.2.3 Isoflurane in general

Isoflurane belongs to the active agent class of the halogenated hydrocarbons. Anaesthesia is achieved by inhalation of the gaseous isoflurane. In Switzerland isoflurane is registered for use in pigs.

3.4.2.3.1 Isoflurane in pigs

A recent study investigated pain and stress levels in piglet castration under isoflurane-anaesthesia (Schulz 2007). Serum-cortisol-concentration was chosen as a parameter representing pain. Cortisol was significantly higher in castrated animals with or without anaesthesia than in animals of the non-castrated control group. Cortisol after castration was significantly lower with an additional application of meloxicam prior to castration. Stress level from castration was evaluated by measurement of plasma-norepinephrine and plasma-epinephrine-concentrations. The concentration of both agents did rise significantly in all piglets handled without anaesthesia independently if castrated or only handled. On the other hand, all norepinephrine and epinephrine-concentrations were significantly lower in anaesthetized animals after castration than before castration. In conclusion, castration under isoflurane anaesthesia reduces stress during castration, but it cannot reduce pain after surgery. Therefore it should be combined with the use of an NSAID postoperative.

The project ProSchwein analysed and tested isoflurane inhalation anaesthesia. 181 piglets were anaesthetized with the inhalation machine of Agrocomp®. It was concluded that with anaesthesia induction time of 90s, 92.3% of the piglets had a sufficient pain relief during surgery. 5.5% of the piglets had a partial success and in 2.2% insufficient pain relief was achieved (Kupper et al. 2008).

3.4.2.3.2 Inhalation machines Pigsleeper® and PorcAnest®

For the inhalation anaesthesia the use of two inhalation machines was tested for the project ProSchwein (Jäggin & Bettschart 2008). The machine Pigsleeper® of the company Schippers® and the machine PorcAnest© of the company Provet® were both proven to fulfil the request for usage for the project ProSchwein. Pain relief was scored in a total of 303 piglets and was found to be adequate in 88% to 100% of the cases tested. The emission at the end of the gas exit was measured and compared to the SUVA (Schweizerische Unfallversicherungsanstalt; Swiss Accident Insurance Fund) guidelines (Kupper et al. 2008). The waste gas needs to be evacuated of the building where the anaesthesia is performed. After filtering the gas, only minimal amounts (< 0.5ppm) of isoflurane were measured (Jäggin & Burren 2008; Jäggin & Burren 2009).

3.4.3 Castration under local anaesthesia

Investigations whether and to what extent local anaesthesia prior to surgical castration can reduce pain were performed, considering physiological response (Prunier et al. 2005), behavioural characteristics (McGlone & Hellman 1988) and vocalisation (Marx et al. 2003).

From 2002 on piglet castration in Norway has been performed only by veterinarians and with the use of local anaesthesia (Fredriksen & Nafstad 2006).

The antinociceptive effect of intratesticular and subcutaneous administration of lidocaine prior to castration was studied (Haga & Ranheim 2005). They concluded that injecting lidocaine into the funiculus spermaticus or into the testes is effective in reducing signs of nociception caused by castration. These authors used electroencephalography (EEG), mean arterial blood pressure (MAP) and pulse rate for assessment of nociception.

Other studies disagree and have shown that local anaesthesia can reduce pain or stress caused by castration to a certain level, but not sufficient to eliminate pain (McGlone & Hellman 1988). Further studies even conclude that castration under local anaesthesia appears to cause pain and stress comparable to that of castration without local anaesthesia (Zols et al. 2006).

In Switzerland the effect of local anaesthesia in piglet castration was studied for the project ProSchwein in collaboration with Agroscope Liebefeld-Posieux. Local anaesthesia reduced the castration pain considerably, but complete pain relief was not achieved and it was concluded that local anaesthesia alone does not accomplish the Swiss standards for pain relief for castration (Jäggin et al. 2008; Kupper et al. 2008).

3.4.4 Anaesthesia by injection

Over the last 20 years variable drugs have been tested for intramuscular or intravenous injection for anaesthesia in the pig. Ketamine is unquestionable the

most important drug in swine anaesthesia, and because its mono-use does produce an insufficient analgesia, it is combined with a wide range of sedatives and analgesic drugs, such as opioids, local anaesthetics or NSAIDS.

3.5 Ketamine

3.5.1 Ketamine in general

3.5.1.1 Pharmacology

Ketamine is an arylcyclohexylamine (Barash et al. 2009). Although ketamine hydrochloride is water soluble, ketamine's lipid solubility is ten times that of thiopentone. The molecular structure (2-(O-chlorophenyl)-2-methylamino cyclohexanone) contains a chiral centre at the C-2 carbon of the cyclohexanone ring so that two enantiomers of the ketamine molecule exist (Reich & Silvay 1989). Of these two optical isomers, the S(+)-ketamine possesses more potent anaesthetic and analgesic effects than the racemic mixture (Barash et al. 2009). Commercially available racemic ketamine preparations contain equal concentrations of the two optical enantiomers, mostly 50:50 mixtures of S(+)- and R(-)-ketamine (Reich & Silvay 1989).

3.5.1.2 Pharmacokinetics

Ketamine has a high bioavailability following intravenous or intramuscular administration. Biotransformation takes place in the liver (Reich & Silvay 1989). Ketamine is mainly metabolized by the cytochrome P450 enzymes to norketamine. This active metabolite norketamine, with an anaesthetic potency one third of ketamine, is excreted by the kidney. Ketamine elimination half-life is 2-4 hours (Reich & Silvay 1989; Barash et al. 2009).

3.5.1.3 Pharmacodynamics

The compound of ketamine interacts with multiple binding sites, including NMDA (N-methyl-D-aspartate) and non-NMDA glutamate receptors, nicotinic and muscarinic cholinergic and monoaminergic and opioid receptors (Kohrs & Durieux 1998). However, the main effect shows ketamine as an NMDA-receptor-antagonist (Kohrs & Durieux 1998; Barash et al. 2009). The NMDA receptor is an ionotropic receptor (ligand gated ion channel) that is activated by glutamate, the most abundant excitatory neurotransmitter in the CNS. The channel is permeable for Ca, Na and K. The NMDA receptor is the postsynaptic site of action in ketamine's reduction of polysynaptic stimulation in the CNS. Ketamine binds to the phenylcyclidine receptor in the NMDA channel and therefore inhibits glutamate activation of the channel in a non-competitive manner. The blockade is time-, concentration-, and stimulation frequency-dependent (use-dependent)(Kohrs & Durieux 1998).

3.5.1.4 Clinical effects

Ketamine belongs to the so-called dissociative anaesthetics. It produces dose-dependent CNS depression with profound analgesia and amnesia. Ketamine

produces a cataleptic state through inhibition of thalamocortical pathways and stimulation of the limbic system (Barash et al. 2009). Ketamine has a cardiovascular stimulatory effect and positive bronchodilator activity (Reich & Silvay 1989; Barash et al. 2009). Protective reflexes such as pharyngeal, laryngeal, eyelid and corneal are present during anaesthesia (Canet & Castillo 2012).
In human medicine, ketamine is mainly used for premedication, sedation and induction and maintenance of general anaesthesia. It is an ideal drug for trauma victims, patients in hypovolemic and septic shock and in patients with pulmonary disease (Schüttler & Schwilden 2008).
In humans, after the sole use of ketamine, adverse reactions such as hallucinations, nightmares, altered cognition and memory, delirium, confusion represent a major problem (Reich & Silvay 1989; Barash et al. 2009). Therefore ketamine should not be administered as a sole agent. The combination with sedative, muscle relaxing drugs will reduce such side effects but not completely abolish them in all patients.
Recently abuse and addiction of ketamine showed to have negative effects upon achievement in education and at work (Morgan & Curran 2011).

3.5.2 Ketamine use in pigs

Ketamine is one of the most important anaesthetic drugs in veterinary clinical practice. Normally it is used in combination with other drugs, because it does not appear to induce surgical anaesthesia when used as a mono-drug. In a survey, a group of experts concluded that ketamine is used with a variety of other drugs such as acepromazine, xylazine, midazolam, diazepam, isoflurane and propofol (Boschert et al. 1996). In properly sedated animals it is suitable for induction and maintenance of anaesthesia. More recently ketamine's use for perioperative pain control has gained widespread popularity in veterinary medicine and it is used as a CRI alone or in combination with other analgesics such as the opioid butorphanol or lidocaine (Larenza et al. 2008b).
With the racemic ketamine pigs may show signs of distress and excited behaviour while recovering from anaesthesia (Ganter et al. 1990; Boschert et al. 1996). Table 1 is giving an overview of ketamine and its combinations that have been studied in pigs.

Table 1 Swine anaesthesia with ketamine for surgical procedures

Literature	Procedure	Animals	Drug	Medication	Route	Effects
McGlone & Hellman 1988	Castration	2 x 18 male crossbred 2 or 7 weeks old	Xylazine Ketamine Glycerol guaiacolate	25ml(500mg) 5ml(500mg) 0.5 mg/kg	IV IV IV	28% death in 2weeks old and suppressed nursing for 3h. Suppressed feeding and drinking times and increased lying times for 6-8h after castration
Ganter et al. 1990			Azaperone Ketamine	2 mg/kg 15 mg/kg	IM IM	Moderate muscle relaxation and analgesia
Nishimura et al. 1992	No surgery, Only anaesthesia		Atropine Xylazine Ketamine - Yohimbin	0.05 mg/kg 2 mg/kg 15 mg/kg 0.05 mg/kg	IM IM IM IM	Anaesthesia 1h, surgical plane only 28 min.
Nishimura et al. 1992	No surgery, Only anaesthesia		Atropine Xylazine Ketamine Butorphanol - Yohimbin	0.05 mg/kg 2 mg/kg 5 mg/kg 0.22 mg/kg 0.05 mg/kg	IM IM IM IM IM	Anaesthesia 1h, surgical plane 68 min. Smooth recoveries, good reversibility with yohimbin.
Sakaguchi et al. 1996	No surgery, Only anaesthesia	18 crossbred piglets, 8-15 weeks old	Atropine Medetomidine Butorphanol Ketamine - Atipamezole	25 μg/kg 80 μg/kg 0.2 mg/kg 10 mg/kg 240 μg/kg	IM IM IM IM IM	Surgical plane for 100 min. Reversible with antagonist atipamezole
Sakaguchi et al. 1996	No surgery, Only anaesthesia	18 crossbred piglets, 8 to15 weeks old	Atropine Xylazine Butorphanol Ketamine	25 μg/kg 2 mg/kg 0.2 mg/kg 10 mg/kg	IM IM IM IM	Surgical plane for 50 min.

Literature	Procedure	Animals	Drug	Medication	Route	Effects
Clutton et al. 1997	Laparoscopy	14 pigs, 10 to 12 months old	Azaperone Ketamine Etomidate Midazolam	1 mg/kg 2.5 mg/kg 200 µg/kg 100 µg/kg	IM IM IV IV	No prevention of motor response to surgery, repeated dosing required
Clutton et al. 1997	Laparoscopy	17 pigs, 10 to 12 months old	Azaperone Ketamine Ketamine Midazolam	1 mg/kg 2.5 mg/kg 2 mg/kg 100 µg/kg	IM IM IV IV	Repeated dosing required
Lahrmann et al. 2005	Castration	1213 male piglets, 5 to 7 days old	Ketamine Azaperone	25 mg/kg 2 mg/kg	IM IM	4% death, but mostly good surgical plan, easy application
Axiak 2007	Castration	40 male piglets 4 to 7days old	Ketamine Climazolam Azaperone	15 mg/kg 1.5 mg/kg 1 mg/kg	IM or IN IM or IN IM or IN	IN shorter recovery than IM. IN less effective anaesthesia
Nussbaumer et al. 2008	Castration, Claw correction Joint tap Radiography Herniorrhaphy	72 crossbred pigs (5kg-265kg) + 3 mini pigs	Romifidine Butorphanol Ketamine	0.12 mg/kg 0.1 mg/kg 8 mg/kg or 5 mg/kg	IM or IV IM or IV IM IV	Surgical plane after 3 (IV) or 10min (IM) after administration. Reliable anaesthesia for 20-30min. Uneventful recovery
Burren et al. 2008	Castration	211 male pigs, 3 to 7 days old	Ketamine Midazolam	15 mg/kg 1.5mg/kg	IM IM	80% sufficient pain relief. Good recoveries. 12 deaths occurred.
Heinonen et al. 2009	No surgery, Only anaesthesia	12 female crossbred, 8 weeks old	Azaperone Detomidine Butorphanol Ketamine	4 mg/kg 0.08 mg/kg 0.2mg/kg 10 mg/kg	IM IM IM IM	Produced deep sedation. No rough recoveries. Only 50% reached surgical plain. Separate injection of agents necessary.
Nussbaumer et al. 2011	Castration	140 male piglets, 10 days to 5 weeks old	Azaperone Butorphanol Ketamine	5 mg/kg 0.2 mg/kg 15 mg/kg	IM IM IM	Good surgical plane, excellent intra-&postoperative analgesia, recovered after 2 h

3.5.3 Ketamine for castration

It was demonstrated that castration is painful and has measurable effects on immediate behaviour in castrated male piglets, compared to their female siblings. Suppression in nursing, drinking and eating was observed and prolonged recoveries. Piglets were anaesthetized with a combination of ketamine, xylazine and glycerol guaiacolate. In the 2-week-old piglets 28% died (McGlone & Hellman 1988).

Ketamine and azaperone were tested intramuscularly with either etomidate/ midazolam intravenously or ketamine/ midazolam intravenously for laparoscopic surgery. With the used doses, most animals responded to surgery and needed additional anaesthetic and the authors concluded that neither of the combinations were ideal anaesthetics (Clutton et al. 1997).

In a large study (Lahrmann et al. 2005) male piglets were castrated with azaperone (2mg/kg) and ketamine (25mg/kg). The induction and recovery phase was uneventful, whereas in the castration phase some animals didn't achieve surgical plane and reacted with defensive behaviour, such as movement or vocalisation. In total 4% death occurred within the first 24 hours, which is most likely due to the high dose of ketamine used in this study.

Intranasal administration of ketamine, azaperone and climazolam was found to produce insufficient anaesthetic depth. Whereas intramuscular injection of those three agents was effective and anaesthesia for castration was found to be consistent and reliable (Axiak 2007).

In a subproject in 2008 an anaesthetic by injection was evaluated with ketamine and midazolam for the project ProSchwein. 80% of the castrates showed a sufficient surgical plane and quality of recovery was good (Burren et al. 2008; Kupper et al. 2008).

Ketamine used at a dose of 10mg/kg with azaperone, detomidine and butorphanol produces good sedation and is useful for minor field surgery, but makes insufficient and unreliable surgical plane in 2 months old pigs (Heinonen et al. 2009).

In a recent study they proved that with a higher dose of azaperone (5mg/kg) in combination with butorphanol (0.2 mg/kg), the ketamine dose could be kept lower and therefore a reduction in the adverse reactions was achieved (Nussbaumer et al. 2011). Most piglets showed no reaction to surgery and all the animals were awake after two hours. The triple combination with butorphanol is a good alternative to the double combination ketamine/ azaperone, as analgesia is better, because of the opioid butorphanol. This method allows the veterinarian to operate on cryptorchids or animals with hernias at the same time (Nussbaumer et al. 2011).

3.6 S-ketamine

In humans it has been noted that S-ketamine produces a more effective anaesthesia and has approximately 4 times higher potency than the racemic ketamine (Reich & Silvay 1989; Morgan & Curran 2011). Other advantages of S-ketamine are less psychomotor side effects and shorter recovery times

compared with R/S-ketamine (White et al. 1985; Koinig & Marhofer 2003). The S-isomer is reported to cause less agitated behaviour and better intraoperative amnesia and analgesia than its enantiomer (Calvey 1995). Clinically S-ketamine is administered at half of the racemic ketamine dose. This is not only associated with a reduction of undesirable adverse effects, but also offers distinctive improvement due to the reduced drug load (Himmelseher & Pfenninger 1998).
Several studies have been performed in animals (table 2).

Table 2 S-ketamine studies in various animals

Species	Literature	Drug	Medication	Route	Effect
Horse	Larenza et al. 2009b: Comparison of anaesthesia recovery quality after racemic (R-/S-) or S-ketamine infusion during isoflurane anaesthesia in horses	Xylazine + R/S-ketamine + Isoflurane + R/S-ketamine or Xylazine + S-ketamine + Isoflurane + S-ketamine	 2.2 mg/kg 1 mg/kg 1.1 mg/kg 0.5 mg/kg	IV IV PI IV IV IV PI IV	S-ketamine better recovery from anaesthesia compared to R/S-ketamine
Syrian Golden Hamster	Erhardt et al. 2001 Comparison of anaesthesia with a combination of racemic ketamine/medetomidine and S-ketamine/medetomidine and antagonising with atipamezole	S-ketamine + Medetomidine + Atipamezole or Racemic ketamine + Medetomidine + Atipamezole	100 mg/kg 0.25 mg/kg 0.25 mg/kg 200 mg/kg 0.25 mg/kg 0.25 mg/kg	IP IP SC IP IP SC	S-ketamine/ medetomidine combination significantly shorter duration of action and less uncoordinated movements than with racemic ketamine/ medetomidine
Goat	Jud et al. 2010 Compare racemic and S-ketamine as induction agents prior to isoflurane anaesthesia. Investigate induction and recovery quality	Xylazine + Racemic ketamine + Isoflurane or Xylazine + S-ketamine + Isoflurane	0.1 mg/kg 3 mg/kg (+/- 0.6mg/kg) 60ml/kg/min 0.1 mg/kg 1.5 mg/kg (+/- 0.3mg/kg) 60 ml/kg/min	IV IV PI IV IV PI	S-ketamine at half the dose rate of racemic ketamine in goats is as equipotent as a induction agent, with the same clinically measurable effects

Species	Literature	Drug	Medication	Route	Effect
Cat	Larenza et al. 2008a Anaesthesia recovery quality after racemic or S-ketamine administration to male cats undergoing neutering surgery	Medetomidine + Racemic ketamine + Atipamezole or Medetomidine + S-ketamine + Atipamezole	30 μg/kg 10 mg/kg 0.15 mg/kg 30 μg/kg 6 mg/kg 0.15 mg/kg	IM IM IM IM IM IM	Faster recovery with S-ketamine at a dose of 60% of racemic ketamine. Tendency towards less behavioural changes in S-ketamine
Dog	Duque et al. 2008 Evaluation of relative potency of racemic and S-ketamine for the hypnotic effect and evaluation of anaesthesia produced by equianaesthetic doses of S- and R/S-ketamine.	Racemic ketamine or S-ketamine	12 mg/kg 12 mg/kg	IV IV	Potency ratio between racemic and S-ketamine 1:1.29, smaller than that reported in other species
Dog	Deleforge et al. 1991 Compare anaesthetic activity of racemic versus S-ketamine to determine advantages of efficacy and tolerance	Racemic ketamine or S-ketamine	10 mg/kg 6.6 mg/kg	IV IV	S-ketamine 3 times more potent than racemic ketamine

Overall, it can be concluded that S-ketamine is equipotent in doses of 50-60% to racemic ketamine. All the studies observed similar anaesthesia induction and maintenance with S-ketamine and some of them confirmed a better recovery phase. Today it is commonly agreed that with S-ketamine at 50-60% of the racemic dose rate desired effects, such as anaesthesia and analgesia, can be achieved, but with less unwanted side effect, such as psychic emergence reactions (Koinig & Marhofer 2003; Schmidt et al. 2005; Larenza et al. 2008b).

3.7 Azaperone

3.7.1 Pharmacology

Azaperone belongs to the neuroleptic agents, belonging to the butyrophenones derivates. Azaperone is chemically known as 4'-fluoro-4-[4-(2-pyridyl)-1-piperazinyl]butyrophenone (Adams 2001).

3.7.2 Pharmacokinetics

Azaperone has a fairly rapid onset following intramuscular injection (5-10 minutes) with a peak effect at approximately 30 minutes post injection (Plumb 2002). The effect lasts about two hours (Heinritzi & König 1988; Plumb 2002). Azaperone is metabolized in the liver with 13% excreted in the faeces. At 16 hours post-dose, practically the entire drug is eliminated from the body (Symoens 1970; Plumb 2002).

3.7.3 Pharmacodynamics

Azaperone as a tranquilizer belongs to the neuroleptic drugs, which have their most prominent effect on the central nervous system. As a neuroleptic agent it blocks dopamine-D_2-receptors and inhibits the release and turnover of dopamine. Dopamine, a catecholamine CNS neurotransmitter is believed to have primary inhibitory activity in the brain, mainly in the basal ganglia and the limbic system (Adams 2001). Azaperone has an antiadrenergic, anticholinerigic, antihistaminic and antidopaminergic effect (Cornick-Seahorn 2001).

3.7.4 Clinical effects

The main effect of azaperone is tranquilization and sedation. It also causes anti-emetic activity, reduced motor activity and inhibition of CNS catecholamines (dopamine, norepinephrine) (Plumb 2002), but has no analgesic effect (Cornick-Seahorn 2001). Azaperone appears to have minimal respiratory effects, and only slight reduction of arterial blood pressure (hypotension) has been measured (Mersmann 1989; Plumb 2002). Other cardiovascular effects include reduction in heart rate (bradycardia)(Mersmann 1989) and cardiac output (Adams 2001).
Adverse reactions like shivering (Plumb 2002), tremors and rigidity (extrapyramidal effect) have been observed (Cornick-Seahorn 2001). Azaperone causes poikilothermia, salivation and hyperpnoea when overdosed (Löscher et al. 2006).

3.7.5 Azaperone use in pigs

Azaperone is used in swine to prevent stress, aggressiveness and fighting that occur when mixing litters (Symoens & Van Den Brande 1969; Gonyou et al. 1988; Adams 2001). It is also used as a general tranquilizer for aggressive sows to allow piglets to be accepted (Plumb 2002). Commonly azaperone is used as sedation prior to general anaesthesia or local anaesthesia (Moon & Smith 1996; Plumb 2002). Sedation seems to be induced smoothly, but lateral recumbency is seldom achieved (Nishimura et al. 1993). After intramuscular injection, pigs should be left undisturbed for 20 minutes (Plumb 2002).

Azaperone is often used in combination with other drugs, such as ketamine (Clutton et al. 1997) or ketamine and climazolam (Axiak 2007), or ketamine, butorphanol, detomidine for anaesthesia under field conditions (Heinonen et al. 2009).

3.8 Butorphanol

3.8.1 Pharmacology

Butorphanol tartrate is a morphine derivate and chemically known as t-N-cyclobutylmethyl-6. It is a partial opiate agonist-antagonist.

3.8.2 Pharmacokinetics

Butorphanol is absorbed completely if administered orally, because of a high first-pass effect, and has also been shown to be completely absorbed following intramuscular injection (Plumb 2002). Butorphanol is metabolized in the liver, mainly by hydroxylation. These metabolites have no analgesic activity and are excreted into the urine (Plumb 2002).

3.8.3 Pharmacodynamics

Butorphanol has an affinity for the μ and κ opioid receptors. Its primary effect at the μ receptor is as an antagonist, and at the κ receptor as an agonist (Adams 2001).

Opioid receptors have been identified within the central and autonomic nervous system, the myenteric plexus of the gastrointestinal tract, heart, pancreas, fat cells, lymphocytes and adrenal glands. The activation of opioid receptors is coupled to changes in ion conductance and G-protein mediated inhibition of cAMP. On a μ receptor this results in an increase of potassium conductance, hyperpolarisation of neuronal membranes and decreasing synaptic transmission. On a κ receptor the G-protein mediated mechanism decreases in calcium influx and neurotransmitter release.

The μ opioid receptors produce supraspinal and spinal analgesia. Kappa (κ) opioid receptors are involved in spinal and supraspinal antinociception. κ agonists produce sedation and dysphoria.

3.8.4 Clinical effects

Butorphanol is mainly used for analgesia (Cornick-Seahorn 2001) and is considered to be 4-7 times more potent than morphine (Adams 2001; Plumb 2002). It is considered to cause mild sedation (Adams 2001; Cornick-Seahorn 2001). Butorphanol possesses significant antitussive activity (Adams 2001; Plumb 2002).
At clinically useful dose rates it induces no unwanted side effects.

3.8.5 Butorphanol use in swine

Butorphanol is licensed for use in horses and minimal residual levels are known. As there are no registered opioids for swine on the swiss market, the use of butorphanol in pigs ("Umwidmung", according to the cascade), is legal.
Butorphanol has often been used in trials to test sedation or surgical anaesthesia for castration (Sakaguchi et al. 1992; Nussbaumer et al. 2008; Heinonen et al. 2009). A triple combination of ketamine, azaperone and butorphanol appeared to have excellent results for castration in piglets where most of the animals showed no reaction to surgical intervention or only mild defensive behaviour. Through using a higher dose of azaperone, the sedative effect was higher and with butorphanol as an analgesic the dose of ketamine could be reduced to 15 mg/kg and therefore no adverse reactions or deaths were observed (Nussbaumer et al. 2011).

3.9 Meloxicam

3.9.1 Pharmacology

Meloxicam is a NSAID – Non Steroidal Anti-Inflammatory Drug, which belongs to the oxicams and therefore to the carboxyl acid derivates (Adams 2001). Chemically known as 4-hydroxy-2methyl-N-(5-methyl-2-thiazolyl)-2H-1,2-benzothiazin-3-carboxamid-1,1-dioxid.

3.9.2 Pharmacokinetics

Meloxicam is well absorbed after oral administration (Adams 2001; Plumb 2002). The drug gets extensively metabolized in the liver to two major inactive metabolites. Excretion is about equally divided between urine and faeces (Busch et al. 1998). Elimination half-life is species specific and there is a significant amount of enterohepatic recirculation (Plumb 2002). Elimination half-life is 8h in mini-pigs (Busch et al. 1998).

3.9.3 Pharmacodynamics

NSAID block the prostaglandin synthesis by inhibiting cyclooxygenase (Adams 2001; Plumb 2002). Prostaglandin can be mediated by either isoform of the cyclooxygenase, COX 1 or COX 2. Prostaglandins generated from COX 1 are constantly present in many tissues including gastrointestinal cells, platelets, endothelial cells and renal cells. COX 2 on the contrary mediate inducible

prostaglandins, which are only needed intermittently (Adams 2001). Meloxicam is considered to be COX 2 preferential.

3.9.4 Clinical effects

Meloxicam is used for treatment of pain and inflammation associated with acute and chronic locomotive disorders and postoperative pain and has analgesic, anti-inflammatory and antipyretic activity (Fosse et al. 2008).
Adverse reactions can be gastrointestinal distress, whereas renal toxicity appears to be quite low (Plumb 2002).

3.9.5 Meloxicam use in swine

Meloxicam is licenced for treatment of chronic pain and locomotive pain. Meloxicam is recommended for relief of postoperative pain such as for example castration in piglets (Keita et al. 2010). In a study with meloxicam the half-life evaluated was 2.7h and the accumulation of the drug in an exudate was shown to be limited. Although, meloxicam is a known COX-2 preferential drug, the study showed that meloxicam inhibits the concentration of PGE_2, which is indicative for COX-2 activity and inhibits $TXB_{2,}$ which is an indicator for COX-1 activity (Fosse et al. 2008). In other trials meloxicam was proven to effectively reduce pain after piglet castration (Schulz 2007; Langhoff et al. 2009; Hansson et al. 2011).

4. Material and methods

4.1 Study design

The experimental trial was designed as a blinded randomised prospective case – control - study according to the guidelines for good clinical practice. The Kanton of Aargau where the experiments took place granted the trials and gave the allowance for an animal trial according to the federal animal protection law. Nine-week-old pigs were castrated under injection anaesthesia either with racemic ketamine or S-ketamine, butorphanol (Morphasol®- 10 ad us. vet., Dr. E. Graeub AG, Berne, Switzerland) and azaperone (Stresnil® ad us. vet., solution for injection, Biokema, Lausanne, Switzerland). During the whole procedure, at predetermined time points, the pigs underwent scoring. Three anaesthesia phases were distinguished: anaesthesia induction (while the pigs were loosing consciousness), anaesthesia during surgery (while getting castrated) and anaesthesia recovery (when the pigs were awakening).

4.2 Farm

The project on castrating 28 male pigs at nine weeks of age could be realised on the farm Aemethof in Densbüren. This is an organic farm with around 100 cows, 30 to 40 calves, 10 heifers, 2 donkeys and 70 to 80 pigs. These fatteners are all from the same breeder. On the Aemethof the fatteners are kept in three different groups of age, consisting each of about 30 animals. The fattening period takes about 100 days, where the pigs stay in the same group until slaughter. The barn is divided in three compartments for the three groups, where each part has its own outside section and can be augmented, while the animals get older. The pigs are fed ad libitum with fattening feed and have access to water at all times.

4.3 Anaesthetic medication

For this study the fatteners were anaesthetized by injection anaesthesia. The intramuscular injection into the neck contained S-ketamine or racemic ketamine and azaperone and butorphanol. All drugs were mixed in one syringe and given together.

4.4 Schedule of events

4.4.1 Group classification A or B

The test drugs S-ketamine and racemic ketamine were provided by Dr. E. Graeub AG in concentrations of 60 mg/ml and 100 mg/ml respectively. The bottles containing the drugs were labelled test drug A or B. Before the experiment a list was prepared and experimental numbers from 1 to 28 were randomly allocated to group A or B. A coin decided which number belonged to which group.

In the morning before the experiment the pigs were separated into smaller groups and coincidentally numbered consecutively. The first group was made up of five pigs, the second, third, forth, fifth and sixth contained three pigs each, and group seven and eight contained four pigs each. One group after the other was brought into the anaesthesia induction box. There the animals were injected at three-minute intervals. When the castration of the last pig of one group was over, the new group was isolated into the anaesthesia induction box and not until then injected with the anaesthetic agents.

4.4.2 Animal selection and identification

28 intact males started their fattening time on the Aemethof on the 1st of September 2010. Coming from the same breeder they on purpose were not castrated as piglets. The animals were all around 63 days of age and in good health condition (no diarrhoea, no cough). They were given one week to get accustomed to the fattening before the experiment. The estimated weight of the pigs was 25 kg bodyweight.
For the test day each pig received a test number from 1 to 28. This number was drawn on to their sides and back with a blue animal marker (LANDI) for proper identification just after the intramuscular injection. When the test animal was brought into the awakening box, the markings were clearly repainted to avoid confusion when retrospectively watching and analysing the videotapes of this phase. During their anaesthesia the eartag/ earmarker was listed and the precise weight was taken by scale (KERN DE60K20NL, Ser No. WC0643834).

4.4.3 Time management

The day before the experiment the free room in the barn outside the stocks was transformed into a simple surgery. One table was used for castration, the other for preparing the medication. The actual daytime was set on the two cameras (SONY, DCR- HC53E and DCR-HC90E) and they were installed in the barn. One camera was recording anaesthesia induction phase, the other registering the recovery phase. Every hour the cassette (SONY Mini DVM 69, LP 90) had to be replaced. The pigs were fed the last time the evening before and were fasted during the night.

4.4.3.1 Three phases

The experiment was divided artificially into three phases:

1. Anaesthesia induction
2. Castration
3. Recovery phase

Every phase had a separate scoring system and during the experiment different timings were recorded. The 28 piglets were separated in small groups to anaesthetize and castrate them shortly one after another. The first group contained five pigs, which were isolated in the anaesthesia induction box. Every three minutes one of them was injected intramuscularly into the neck. The IM time was recorded and the camera was on. After 15 minutes, the first pig was assessed and while sleeping scrubbed for surgery. After or just before castration,

every experimental animal was weighed. The castration was performed through residents of the Section of the Swine Clinic, Department of Farm Animals, Veterinary Faculty University of Zürich, Switzerland and students who were instructed by swine specialists of the swine section. While test animal number 1 got castrated, pig number 2 got scrubbed for surgery and so on until all the group members were castrated. After five castrations the used set of instruments was sterilised in a bowl of Cidex10% (Gigasept® FF, Schülke & Mayr AG, Zürich, Switzerland) and meanwhile a new sterile set was used. To recover from anaesthesia, each fattener was laid in the recovery straw box, which had video surveillance. As soon as one test animal was able to stand it was brought into another box, so the still unconscious pigs were less disturbed. Every pig underwent the same procedure. At the end of the test day, all castrates were returned to their compartment of the barn and were allowed access to food and water.

4.5 Anaesthesia and analgesia

To test the action of S-ketamine the pigs were anaesthetized by an intramuscular combination of three agents: 5 mg/kg azaperone, 0.2 mg/kg butorphanol and 15 mg/kg racemic ketamine or 9 mg/kg S-ketamine. The mixture was applied intramuscularly into the neck. In addition, the non-steroidal anti-inflammatory drug meloxicam (Metacam®- 20 mg/ml ad us. vet., Boehringer Ingelheim GmbH, Basel, Switzerland) was administered IM in a dose of 0.4 mg/kg and tetracyclinespray (Chlor-Tetracycline-Spray Stricker ad us. vet., Werner Stricker AG, Zollikofen, Switzerland) administered locally after castration. All animals were initially medicated with exactly the same dose, estimating the bodyweight at about 25 kg.

4.5.1 Anaesthetic depth

The anaesthetist decided according to a predetermined score when the pigs needed further medication.

- Firstly, if an animal did not get into stage of immobility after its intramuscular injection. It was re-dosed further with ½ the initial dose, that being 2.5 mg/kg azaperone and 7.5 mg/kg racemic ketamine or 4.5 mg/kg S-ketamine intramuscularly.
- Secondly if a pig reacted to the first touch and pinching the nasal septum or other external influences in the castration phase (washing, weighing, castrating) it was dosed further with ¼ the initial dose, according to group A or B either 3.75 mg/kg racemic ketamine or 2.25 mg/kg S-ketamine intravenously into an ear vein. After one dose the pig was left to relax for 45 seconds before testing the anaesthesia again by pinching into the nasal septum. If reaction occurred another ¼ dose of ketamine was applied, till there was no more reaction to the pinching.
- Thirdly, if a test candidate reacted to the pinching of the spermatic cord or to the pulling out of the testicle, lidocaine 2.5 ml for each aching spermatic cord (Lidocain HCl 2%, Kantonsapotheke Zürich, Switzerland) was injected directly into the spermatic cord.

4.6 Castration

From the anaesthesia induction box, the pig was brought to a wooden pallet. There it lied in dorsal recumbency. The animals testicles and surrounding got scrubbed twice with betadine soap (Betadine® fluid soap, Provet. AG, Lyssach, Switzerland) and water. The area to scrub was from between the hind legs to above the anus. To degrease the surgical field ethanol ("Ethanol ketoniert 80% V7V KA", Kantonsapotheke Zürich, Switzerland) was used. With betadine solution (Betadine® standardised solution ad us. vet., Provet. AG, Lyssach, Switzerland) the surgical field was disinfected.
The surgeon scrubbed her-/himself with betadine fluid soap and put on a pair of sterile gloves (Sempercare® edition, IVF Hartmann AG Neuhausen, Switzerland). In the meantime, the pig was carried to a table, which was covered with a surgical drape (Convertors®, Cardinal Health, Dublin, Ireland). There it lied in dorsal recumbency. The pig was not restrained at any point. An experienced anaesthetist (Regula Bettschart-Wolfensberger) was placed at the head of the animal to register reactions with the head or listen to a noise to be able to top up the medication. Another person was holding and spreading the back legs, so the surgeon had a good view and sufficient space to castrate the fattener.
To process the first cut, the testis was moved with the thumb into a position, so that the skin over the testis was under tension. Then a long cut with a scalpel blade was made to press the testis through the incision. The tunica vaginalis was not cut open. The testis was separated from the scrotum with traction. The spermatic cord was pulled out and the forceps was positioned on the spermatic cord close to the abdominal wall. Below the forceps a fibre (Biosyn®, 3 metric, Syneture™, Dublin, Ireland) was knotted and the testis and part of the spermatic cord was removed. The second testis was handled the same way. At the end the two incisions were sprayed with tetracycline. The pig was moved into the recovery box and was left undisturbed. There it was put on pulp with its distal body region and lied in lateral recumbency.

4.7 Time recording

Every animal had its own stopwatch and protocol. With the initial intramuscular injection of azaperone, butorphanol and ketamine, the actual daytime was recorded and the stopwatch was started immediately. The phase of anaesthesia induction was videotaped. Three timings were read off the stopwatch through this phase.

1. tF: The first time the pig got into sternal recumbency.
2. tG: The pig stayed in lateral recumbency without getting up again.
3. tH: The pig showed no more movement - stage of immobility.

After 12 to 15 minutes the animal was assessed for the first time after injection, meaning it was touched (A) and pinched into the nasal septum. From then on, every timing was recorded directly, without using a camera. Another time point was when the animal was brought onto the surgery table and put into dorsal

recumbency (B). Then the first cut (C1), the first pinching off spermatic cord (D1), the second cut (C2), the second pinching off spermatic cord (D2) was recorded. The time was written onto the sheet when the castration was over (E). This was when the tetracycline spray was applied and the pig was removed from the surgery table and brought into the recovery box. The duration of the castration was calculated from the first cut (C1) to the end of the castration (E).
Additionally, timings of all further doses of medication during the procedure were recorded.
In the recovery box a camera observed all the pigs while waking up. The camera was attuned to the actual daytime, so all the tapes were labelled. In this phase the time was noted on 3 occasions.

1. tK: The first movement was registered.
2. tL: The first time sternal recumbency was achieved, even if it lied down again.
3. tM: Ability to stand: has to walk at least 4 steps without tilting over.

These times were calculated retrospectively from the starting time of the injection on the protocol sheet and from the videotapes showing the daytime.

4.8 Scoring

4.8.1 Anaesthesia induction

Every animal had its own protocol sheet with the timing and the scoring on it. The scoring for the anaesthesia induction phase was evaluated afterwards from the videotape. The camera recorded every group till the last animal was immobile. Three parameters were observed and scored: ataxia, rowing and lying down & getting up. Each parameter was scored separately from 0 - 3 and was independent from the timing in this phase.

Table 3 Scoring for induction phase

Score	Ataxia	Rowing	Lying down, getting up
0	No ataxia	No rowing	None and 1 x getting up
1	Ataxia once	Rowing once	>1 x getting up
2	Ataxia repetitively	Rowing repetitively	>3 x getting up
3	Ataxia continuously	Rowing continuously	>6 x getting up

4.8.2 Castration

The scoring is in relation with the timing. At the specific points in time (A, B, C1, C2, D1, D2), mentioned previously, the reaction of each pig was scored. The parameters used were the same for every judgement: quantity of movements, intensity of movements, vocalisation. The scoring ranged from 0 – 4 and is listed in table 4. See annexe for original table.

Table 4 Scoring for castration linked to certain time points

Score	Quantity of movements	Intensity of movements	Vocalisation
0	No movement	No movement	No vocalisation
1	Movement once	Movement of one extremity	Vocalisation once
2	Movement repetitively	Movement of more than one extremity	Vocalisation repetitively
3	Movement continuously	Spinal cord inclusive	Vocalisation continuously
4		Like 3, but stronger	

4.8.3 Recovery phase

The scoring of this phase was independent of time. The evaluation was realised by watching the videotapes after the test day. The whole day a camera was recording the recovery phases of the castrates. Every 60 minutes the tape was changed. The scoring was composed of three parameters: Rowing, convulsions, attempts to get up. During the whole phase the test animal was observed and scored in each parameter from 0 - 3.

Table 5 Scoring for recovery phase

Score	Rowing	Convulsion	Attempt to get up
0	No rowing	No convulsion	One attempt
1	Rowing once	One convulsion	> 1 attempt
2	Rowing repetitively	Convulsions repetitively	> 3 attempts
3	Rowing continuously	Convulsions continuously	> 6 attempts

4.9 Statistics

Statistical analysis was performed with the program STATA® (StataCorp., 2009; Stata Statistical Software: Release 12.0; College Station, TX, USA: StataCorp LP).
To analyse the timings in relation to the group S-Keta and Keta-Race a T-test and and ANOVA for repeated recovery time data was used. Concerning additional doses a chi square test was used and the scoring was analysed by two sample Wilcoxon rank-sum test.
To rule out differences between timing and scoring within the castration phase, because they were linked to each other, a logistic regression with the co-variable time was used.
The cut off for significance was set at $p \leq 0.05$ and a p-value between >0.05 and 0.2 was recorded as a tendency.

5. Results

5.1 In general

All 28 fatteners survived the anaesthesia and were successfully castrated. There was no difference between the two groups concerning scaled body weight (mean weights: S-Keta 26kg, Keta-Race 25kg). The mean total dose rates in ml of the test drugs were statistically not different S-Keta 5.42 ml/pig and Keta-Race 5.16 ml/pig. Mean duration of surgery was not different between both groups (S-Keta 571 secs, Keta-Race 642 secs).

5.2 Exclusions

Only a part of the recorded data in two animals could be used, because they were re-dosed with the wrong ketamine.

5.3 Anaesthetic depths and analgesia

Two animals in the S-Keta group were not sufficiently anaesthetized in the induction phase which was defined as not reaching immobility (tM) and were re-dosed with ½ the initial dosages of azaperone and the test drug (S-ketamine or racemic ketamine) intramuscularly.

After reaching the state of immobility, each pig would be touched, pinched into the nasal septum and transported to get ready for castration. In this castration phase 23 out of the 28 fatteners had to have their anaesthesia deepened by intravenous administration of ¼ of the initial dosage of S-ketamine or racemic ketamine. 13 pigs in the S-ketamine group on 25 occasions and 10 pigs in the group Keta-Race on 21 occasions needed re-dosing. Most of the top-ups where administered between tA: first touch and tB: moving onto surgery table. Only three pigs needed further anaesthetics while being castrated (tC1- tE). In table 6 the number of fatteners that needed top-up with ¼ of the initial dosage of ketamine are listed. Additionally it shows how many animals needed re-dosing once, twice, three times or even four times. There was no difference between the groups.

Heavier fatteners needed significantly more supplemental racemic or S-ketamine.

5.3.1 Re-dosing

Table 6 Re-doses for S-Keta or Keta-Race with ¼ initial ketamine dose intravenously

¼ Ketamine	Yes	No	Total	0x	1x	2x	3x	4x	Total
S-Keta number of animals	13	1	14	1	4	7	1	1	25
Keta-Race number of animals	10	4	14	4	3	4	2	1	21
Total of animals	23	5	28	5	7	11	3	2	28
Total of re-dosages				0	7	22	9	8	46

5.3.2 Local anaesthesia

Local anaesthesia with lidocaine was done only if necessary. In both groups three fatteners needed one injection (one testicle) of lidocaine, and in group S-Keta two animals had both testicles injected.

Table 7 Lidocaine use while castration was performed

Lidocaine	2.5 ml	5 ml	Total
S-Keta	3	2	5
Keta-Race	3	0	3
	6	2	8

5.4 Timing

5.4.1 Induction phase

Three animals were not immobile after 15 minutes, which was interpreted as an insufficient anaesthetic depth. In the anaesthesia induction there was a tendency for the Keta-Race group to be faster in sternal and lateral recumbency (tL), after a mean of 253s (with a 95% confidential interval of 177- 330s) compared to S-Keta 602s (with a 95% confidential interval of 152- 1051s).

Table 8 All the timings throughout the induction, castration and recovery phase for both groups

Timing	S-Keta		Keta-Race		p-value
	„mean“ in s	min.s	„mean“ in s	min.s	
tK: 1. sternal recumbency	200	3.20	127	2.07	0.07
tL: Lateral recumbency	602	10.02	253	4.13	0.14
tM: Immobility	629	10.29	458	7.38	0.36
tA: 1. touch	1229	20.29	1285	21.15	0.80
tB: Onto surgery table	1605	26.45	1577	26.17	0.91
tC1: 1. cut	1799	29.59	1720	28.40	0.78
tD1: 1. pinching off SC	1930	32.10	1782	29.42	0.63
tC2: 2. cut	2182	36.22	2075	34.35	0.74
tD2: 2. pinching off SC	2308	38.28	2174	36.14	0.66
tE: End of castration	2381	39.41	2367	39.27	0.96
tC1-tE: Castration duration	571	9.31	642	10.42	0.24
tF: 1. movement	3304	55.04	3570	59.30	0.43
tG: 1. sternal recumbency	4258	70.58	4675	77.55	0.16
tH: Ability to stand	6006	100.06	6483	108.03	0.25

SC: spermatic cord

5.4.1.1 Group 1 to 8: injection order in smaller groups and correlation with induction phase

The 28 pigs were divided into smaller groups to get injected with the anaesthetic agent. This group each contained between three to five pigs. In the anaesthesia induction phase the fatteners were injected intramuscularly at three-minute intervals. Statistically, it could be ruled out that the order in which the animal was injected had an influence on its anaesthesia induction timings (tK first sternal recumbency, tL lateral recumbency or tM immobility).

5.4.2 Castration phase

There was no difference in timings from first touch to end of castration (tA to tE) between the two groups and neither was duration of castration different between the groups. On average, the test animal received its first touch after IM injection at 20 or 21 minutes and was moved into the recovery box (tE) after 39 minutes.

5.4.3 Recovery period

In the recovery phase first movements (tF) were observed earlier in the S-Keta group (3304s with a 95% confidential interval of 2793 - 3815s) compared to Keta-Race group (3570s with a 95% confidential interval of 3051 - 4090s). There was also a tendency that animals in the S-Keta group are faster in their first time in sternal recumbency (tG), S-Keta 4258s (70.58min): Keta-Race 4675s (77.55min). Furthermore, fatteners of the S-Keta group were able to stand up (timing tH) after 6006s, which is 8 minutes quicker in comparison to the pigs in the Keta-Race group (6483s). General anaesthesia time was therefore 100

minutes (1 hour and 40minutes) in S-Keta group or 108 minutes (1 hour 48 minutes) in Keta-Race group. All three timings comparing S-Keta with Keta-Race are presented in figure 1.

Figure 1 S-Keta pigs compared to Keta-Race animals reached each timing earlier (first movement, first sternal recumbency and ability to stand)

5.4.3.1 Correlation tE end of castration and tF first movements

The sooner a castration was finished, the earlier the animal showed its first movements in the recovery box. No group difference exists between S-Keta and Keta-Race.

Figure 2 End of castration tE is shown as red bar and ranges from 26 minutes to 73 minutes with a mean of 40 minutes. Every green dot equals one fattener. Significant correlation, the earlier tE, the sooner tF.

5.4.3.2 Correlation re-dosing and timings in recovery phase

A significant correlation between re-dosing and recovery phase was noted. The more top-ups the pigs in the S-Keta group had, the earlier they were in first sternal recumbency (tG), but the more re-doses the animals in the Keta-Race group had, the later they were in first sternal recumbency (tG). The more supplemental racemic ketamine the pigs of the Keta-Race group got, the later they showed first movements (tF) or ability to stand (tH), whereas the more supplemental S-ketamine the S-Keta group fatteners received, the earlier they made their first movements or were able to stand.

5.5 Scoring

5.5.1 Induction phase

No differences were evaluated between the two groups in the measurements ataxia, rowing and lying down & getting up. The scores are listed in table 9. The figure 3 shows an example of the distribution of the scoring ataxia, with S-Keta and Keta-Race. The observation for the score rowing was as followed: 10 animals of the S-Keta group were not rowing throughout induction, one animal rowed once, two animals rowed repetitively and one animal showed continuously rowing. Six animals of the Keta-Race group showed no rowing, six animals rowed once, one pig rowed repetitively and one pig showed continuous rowing.

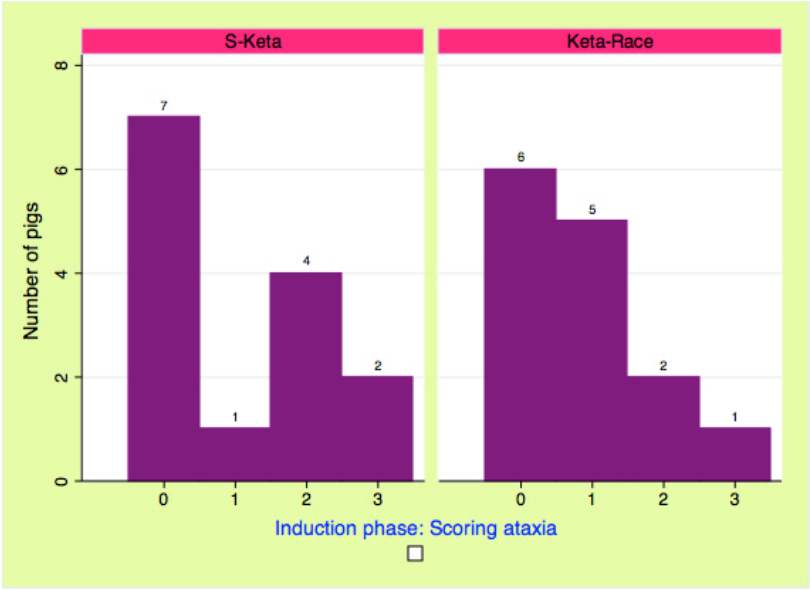

Figure 3 Score ataxia in the anaesthesia induction phase is distributed evenly between the two groups S-Keta and Keta-Race

5.5.2 Castration phase

On defined timings through the castration the quantity of movements, the intensity of movements and vocalisation were scored. There were no significant differences between the two groups S-Keta and Keta-Race. Overall, most fatteners reacted with movements at tA (first touch and nasal septum pinch) and tB (moving onto surgery table). After one or several top-ups with ¼ dose of S-

ketamine or racemic ketamine, the pigs then seemed to have a good anaesthesia and analgesia and showed less quantity and therefore quality of movements. Timing tD1, pinching off first spermatic cord, and tD2, pinching off second spermatic cord, provoked one or repetitive movements, whereas cutting the skin released fewer reactions. At the timing tD2, where the second spermatic cord gets crushed, three animals of the S-Keta group showed once or repetitive vocalisation.

Table 9 All scores on induction, castration and recovery phase are listed below including the p-value

Scoring	**Ataxia**					**Rowing**						**Lying down & getting up**				
Scores	**0**	**1**	**2**	**3**	**p**	**0**	**1**	**2**	**3**		**p**	**0**	**1**	**2**	**3**	**p**
Total	13	6	6	3	0.75	16	7	3	2		0.29	16	5	6	1	0.76
S-Keta	7	1	4	2		10	1	2	1			9	1	3	1	
KetaRace	6	5	2	1		6	6	1	1			7	4	3	0	
	Quantity of movements					**Intensity of movements**						**Vocalisation**				
Scores	**0**	**1**	**2**	**3**	**p**	**0**	**1**	**2**	**3**	**4**	**p**	**0**	**1**	**2**	**3**	**p**
tA total	9	5	9	4	0.69	11	0	8	7	1	0.92	27	0	0	0	-
S-Keta	3	4	4	2		5	0	4	4	0		13	0	0	0	
KetaRace	6	1	5	2		6	0	4	3	1		14	0	0	0	
tB total	13	5	6	3	0.36	15	0	7	3	2	0.87	26	0	1	0	0.30
S-Keta	5	3	3	2		7	0	3	3	0		12	0	1	0	
KetaRace	8	2	3	1		8	0	4	0	2		14	0	0	0	
tC1 total	23	3	0	0	0.55	23	1	2	0	0	0.49	25	1	0	0	0.32
S-Keta	11	2	0	0		11	0	2	0	0		12	1	0	0	
KetaRace	12	1	0	0		12	1	0	0	0		13	0	0	0	
tD1 total	18	8	0	0	1.00	19	4	3	0	0	0.79	25	1	0	0	0.32
S-Keta	9	4	0	0		10	1	2	0	0		12	1	0	0	
KetaRace	9	4	0	0		9	3	1	0	0		13	0	0	0	
tC2 total	22	4	0	0	0.29	22	2	2	0	0	0.33	25	1	0	0	0.32
S-Keta	10	3	0	0		10	2	1	0	0		12	1	0	0	
KetaRace	12	1	0	0		12	0	1	0	0		13	0	0	0	
tD2 total	14	10	2	0	0.30	15	2	9	0	0	0.22	23	2	1	0	0.07
S-Keta	6	5	2	0		6	1	6	0	0		10	2	1	0	
KetaRace	8	5	0	0		9	1	3	0	0		13	0	0	0	
	Rowing					**Convulsion**						**Attempt to get up**				
Scores	**0**	**1**	**2**	**3**		**0**	**1**	**2**	**3**			**0**	**1**	**2**	**3**	**p**
Total	22	2	2	0	0.25	20	3	3	0		0.92	0	4	6	16	0.77
S-Keta	12	1	0	0		10	2	1	0			0	3	2	8	
KetaRace	10	1	2	0		10	1	2	0			0	1	4	8	

5.5.3 Recovery phase

5.5.3.1 Rowing

Although, there was no significant statistical difference noted between the S-Keta and the Keta-Race group, two pigs in the Keta-Race group showed repetitive rowing when waking up. The rowing was extensive and could be described as heavy paddling with all four legs.

5.5.3.2 Convulsion

Continuous convulsion was never observed in the recovery phase. A single convulsion/ muscle fasciculation was noted in two animals of the S-Keta and one

pig in the Keta-Race group. Repetitive convulsions were noted in one animal of the S-Keta and two animals of the Keta-Race group.

5.5.3.3 Attempt to get up

The number of attempts to get up before able to stand properly was distributed evenly between the two tested groups.

5.6 General other observations

Tongue-movement and shaking was observed in six animals and was recorded on the sheets. Nine pigs reacted with movement of their head while being castrated. Some fatteners expressed themselves by grunting or wheezing, which was not scored as a vocalisation.

5.7 Post-treatment remarks

None of the fatteners developed surgical site infection. At a re-visit on the farm one, three and five days after castration all the fatteners behaved normally. One animal had a swollen scrotum, which looked fluid filled (seroma). After discussion with the farmer it was agreed to observe the animal for appetite, general behaviour and decrease of the scrotal seroma. The seroma resolved without external influences.

No further problems were reported and the fatteners were slaughtered at the age of approximately 100 days.

5.8 Costs

Table 10 Prices of drugs

Substance	Medicament	Amount per bottle	Price per bottle	Price per ml	Dose/ animal	Dose in ml per kg	Price per kg	Price for 25kg (9-week-old)
Azaperone	Stresnil, 40 mg/ml	100ml	75.70CHF	-.75CHF	5mg/kg	0.125 ml	-.09CHF	2.34CHF
Butorphanol	Morphasol-10, 10mg/ml	20ml	192.-CHF	9.60CHF	0.2mg/kg	0.02ml	-.20CHF	4.80CHF
Ketamine	Ketasol-100, 100mg/ml	50ml	73.-CHF	1.46CHF	15mg/kg	0.15ml	-.22CHF	5.48CHF
Ketamine	Keta-S, 60mg/ml	10ml	55.30CHF	5.53CHF	9mg/kg	0.15ml	-.83CHF	20.74CHF
Meloxicam	Metacam, 20mg/ml	100ml	99.85CHF	-.99CHF	0.4mg/kg	0.02ml	-.02CHF	-.50CHF
Lidocaine	Lidocaine HCL 2%, 20mg/ml	100ml	7.30CHF	-.07CHF	2.5ml or 5ml			-.18CHF or -.35CHF

The price per kg is -.53CHF per animal with racemic ketamine and 1.14 CHF for S-ketamine.
The cost for injection anaesthesia with the drugs used in this study for 9 weeks old fatteners, with a bodyweight of around 25kg adds up to 13.12 CHF for using racemic ketamine or 28.38 CHF when using S-ketamine. If lidocaine is needed, there will be an extra cost of 0.18 CHF for injecting one testis, or -.35 CHF for injecting two testes.
Additionally to the drug costs, will be the veterinary visit fee, but mostly the veterinarian might be able to combine the call and treat other animals on the farm.

Comparing the two methods inhalation and injection anaesthesia with each other, a few facts need to be considered.
The costs for buying an inhalation machine are very high, ranging from 5000.- to 12'000.- CHF with additional fees for each isoflurane bottle. A farmer does need to castrate a lot of pigs to validate/amortise a machine or needs to share the infrastructure with other farms. Additionally though administration of a pain relief such as meloxicam is mandatory.
Injection anaesthesia on the other hand has no machine to buy. However, for each castration procedure a veterinarian has to visit and inject every piglet. Intravenous injection can normally not be delegated to the farmer.

Table 11 Costs of isoflurane inhalation machines

Company	Machine	Price in CHF
MS Schippers GmbH	MS Pigsleeper® combi	9000.-
Agrocomp	PIGNAP® Pro/Light/Easy	9300.- to 12000.-
Provet	Porc-Anest®3000	8500.-
Provet	Attane™ Isofluran 250ml	110.-

6. Discussion

The present study tested the use of S-ketamine at a dose rate of 60% of the racemic ketamine in comparison to racemic ketamine for castration of 9-week-old pigs. In order to induce satisfactory anaesthesia the ketamines were combined with azaperone, butorphanol and meloxicam. Where analgesia seemed inappropriate, local anaesthesia was applied in the anaesthetized pig. Overall, S-ketamine at that dose rate induced anaesthesia comparable to racemic ketamine. A high number of animals in both groups needed supplemental ketamine and/or local anaesthesia to achieve satisfactory anaesthesia. Considering the fact that dose rates on the high end of published data were used this was surprising. Many studies are warranted to optimise anaesthesia for castration of piglets.

Comparative studies between racemic ketamine and S-ketamine have been performed in other species than pigs. In most studies dose rates of 50 or 60% of the racemic ketamine dose for S-ketamine were chosen and considered equipotent (Deleforge et al. 1991; Larenza et al. 2008a; Larenza et al. 2009b; Jud et al. 2010). In the present study 60% of the racemic dose was chosen for S-ketamine to compare its effect with those of R/S-ketamine. No anaesthetic death was recorded and the 28 male fatteners all recovered well from intramuscular injection anaesthesia.

The dose used in this study was 15 mg/kg racemic ketamine or 9 mg/kg S-ketamine. The dose rate for the racemic ketamine was chosen based on published data of Nussbaumer et al (Nussbaumer et al. 2011).
The pigs weight was estimated as being 25 kg bodyweight and the assessment of the scaled weight revealed that there were no statistical differences between the groups. The need for re-dosing was evenly distributed throughout the treatment groups with a mean dose of 13mg/kg S-ketamine and 20mg/kg racemic ketamine. The dose range of racemic ketamine used in other studies varies from 8mg/kg to 25mg/kg (Boschert et al. 1996; Lahrmann et al. 2005; Axiak 2007; Nussbaumer et al. 2008; Heinonen et al. 2009). In the newest study in Switzerland Nussbaumer et al (Nussbaumer et al. 2011) successfully castrated 140 piglets with the intramuscular injection of 5 mg/kg azaperone, 0.2 mg/kg butorphanol and 15 mg/kg ketamine. They concluded that the triple combination induced successful anaesthesia and analgesia and that the preferred age for castration with this combination would be three weeks.
In the current study most pigs (23 out of 28) needed further doses of racemic or S-ketamine on a total of 48 occasions and the initial dose of racemic and S-ketamine was insufficient to provide satisfactory anaesthesia. One possible explanation for the differences to Nussbaumer et al's study (Nussbaumer et al. 2011) could be the age of the test animals, which was 9 weeks, and therefore older than in most castration-trials. Furthermore, another explanation is that different teams performed the studies with maybe different attitudes towards judgement of depth of anaesthesia.
Most animals needed a top-up with ¼ the initial dose of racemic or S-ketamine when first touched (tA) or prepared for surgery (tB). Once the pigs were on the surgery table, the anaesthesia was found to be satisfactory and only eight pigs had to have lidocaine injected into their testis.

To objectively evaluate the anaesthetic and analgesic state of the tested pigs, certain time-points throughout the anaesthetic were predefined. Scores were designed for judgement of quality of anaesthesia and analgesia, induction and recovery (at the predetermined different time-points). Several studies results were combined to design these scores (Nishimura et al. 1993; Heinonen et al. 2009; Leidig et al. 2009).

The timing during the induction phase was useful in assessing how fast animals would be anaesthetized, which is an important factor when castrating piglets. We found that the mean time with our 9-weeks-old pigs for immobility tM was 10 min 29 s for S-Keta and 7 min 38 s for Keta-Race pigs. This is similar to the 5 to 10 minutes in Nussbaumer et al's study (Nussbaumer et al. 2011). Although there was no statistical difference between the timings in the induction phase and the order the fatteners were injected intramuscular, the author observed a lot of disturbance through external stimuli. Some animals reacted wildly to a companion shrieking when getting injected, and others even stood up and fled. Because of the age and weight of the pig it would have been ideal to separate each animal after IM injection to make objective undisturbed observations. But we refused to do so, as we wanted to mimic field conditions. The scores in the induction phase were evenly distributed between the two tested groups for ataxia, rowing and lying down & getting up again. Even though a few candidates showed anaesthesia inductions that were subjectively not satisfactory, this was not reflected in the scoring. Some pigs tried to climb the walls and did summersaults. This was not included in the scoring. The use of a visual analogue scale in future studies would certainly improve judgement of quality of anaesthesia induction.

The timing and scoring during castration was linked. At every time-point the scoring had to be accomplished. For the current study of important value was that there were no significant differences in timing or scoring between the S-Keta and racemic group. This period started with the first touch tA and ended with tE the end of the castration and the application of tetracyclin spray and moving into the recovery box. Movements and vocalisations were scored. Scoring problems aroused when animals only twitched, but did not actually move a body part or if they only moved their head (without any limbs) or twitched their tongue. These values were observed, noted, but not included in the predetermined score. In a next study these events should be included into the score in order to improve the quality of judgement.

During recovery there was a significant correlation between time of sternal recumbency and re-dosing. The pigs in the S-Keta group reached all time-points in recovery earlier, compared to the pigs in Keta-Race group, where the animals with more re-doses took even longer to recover. S-ketamine fulfilled our expectations concerning recovery times: first movements after 55 min (4 min earlier than Keta-Race), first sternal position after 71 min (7 min earlier than Keta-Race) and ability to stand after 100 min (8 min earlier than Keta-Race). This faster recovery with S-ketamine has also been noted in other species and occurred due to faster elimination of the S-isomer when used as a single agent

compared to its use within the R/S-ketamine. In Shetland Ponies time to standing position after anaesthesia was significantly diminished after S-ketamine compared to R/S-ketamine (Larenza et al. 2008b; Larenza et al. 2009a). In cats undergoing neutering it was observed that anaesthesia with S-ketamine, at 60% of the R/S-ketamine dose, provided faster recoveries (Larenza et al. 2008a).
To score the recovery following parameters were used: rowing, convulsion and how many attempts a pig needed to get up. Concerning rowing and convulsion, the intensity was not scored. Retrospectively this scoring system seems not precise enough to the authors. Nevertheless, two fatteners in the Keta-Race group showed repetitive rowing, which could be described as extensive, severe paddling with all four limbs, which was not registered in the S-ketamine group. However, the number of total convulsions and attempts to rise was identical in both groups. Better recovery qualities with S-ketamine were also published in cats, horses and syrian golden hamsters (Erhardt et al. 2001; Larenza et al. 2008a; Larenza et al. 2009b).

According to the law in Switzerland every animal has to be anaesthetized for castration since January 2010 (BVET 2009).
According to the EU legislation, castration after seven days of life shall only be performed under anaesthesia and additional prolonged analgesia by a veterinarian. The project PIGCAS focused on attitudes, practice and state of the art regarding piglet castration across European countries. In the majority of the European countries piglet castration is performed without anaesthesia. The study reasons that the collected data in PIGCAS reveals inconsistency between current practice and EU legislation. They concluded that about 250 million pigs are slaughtered in Europe each year. Of the 125 million male pigs approximately 20% are left entire, less than 3% are castrated with anaesthesia and the rest (77%) without anaesthesia. Raising entire males is much less common and only a few countries find it possible not to castrate, for example Ireland and United Kingdom, and a decreasing number of animals in Spain and Portugal. Castration with anaesthesia is mandatory in Norway, where piglets are castrated with local anaesthesia. In the Netherlands they are aiming for abandoning castration without anaesthesia (Fredriksen 2009).
Before the law came into effect, the Swiss College of Agriculture SHL launched a project called ProSchwein, which investigated all the possible methods of anaesthesia for castration, methods without castration, acceptance of alternative methods, economical impacts and international developments.
Local anaesthesia injection was found not to achieve complete analgesia and does on its own not accomplish swiss standards for pain relief for castration (Jäggin et al. 2008; Kupper et al. 2008). Further studies even conclude that castration under local anaesthesia appears to cause pain comparable to that of castration without local anaesthesia (Zols et al. 2006).
By using isoflurane inhalation anaesthesia for piglet castration several factors need to be taken into consideration. Farmers have to gain a diploma before they are allowed to castrate piglets using isoflurane anaesthesia (BVET 2009). One needs to be aware of the risks of incorrect use of the anaesthetic machine and the possible pollution of incorrect outlet of the waste gas (Jäggin & Burren 2008; Kupper et al. 2008; Jäggin & Burren 2009). Because isoflurane itself is not

analgesic additional pain relief needs to be administered intramuscularly, such as the NSAID meloxicam (Schulz 2007).
Successful trials were performed with vaccination against boar. This method requires good vaccination procedures and management practices on the farm. The quality control at the slaughter chain requires extra control steps, however, it can limit the chance to a minimum, that tainted meat could reach the market chain.
Some entire males were fattened experimentally and none of the slaughtered carcasses was found to test positive for boar taint with the cooking test.
A large survey conducted in the Swiss market revealed better client acceptance for surgical castration compared to vaccination against boar taint (Kupper et al. 2008; de Roest et al. 2009). Additional information to the vaccination method did improve the later acceptance, showing that proper information is needed to introduce new methods (Kupper et al. 2008).

Since implementation of the law in Switzerland in 2010 some farmers use isoflurane inhalation anaesthesia and other farmers get the veterinarian to inject their piglets for anaesthesia with a combination of azaperone/ butorphanol/ ketamine intramuscularly after a recommendation of the Swiss Society for Pig Medicine (SVSM).

The present study showed that 9 mg/kg S-ketamine in combination with 5 mg/kg azaperone and 0.2 mg/kg butorphanol produces a surgical tolerance level of anaesthesia in pigs, comparable to 15 mg/kg R/S-ketamine in combination with the same drugs, but a lower incidence of untoward effects during and a faster recovery phase. S-ketamine for pigs is useful if a smooth and quick recovery is mandatory. The present study also showed, that with both ketamines the number of re-doses necessary to induce acceptable anaesthesia quality to allow surgery, was high despite the fact, that dose rates in the higher range of published doses were used.
As surgeries under field conditions such as castration, scrotal or umbilical hernia repair, caesarean section, claw amputation, atresia ani correction and uterus prolapse surgery (Lahrmann 2006) are common in pigs, the need to find safe and cost effective drug combinations is major.

7. Content of tables and figures

7.1 Tables

7.2 Figures

8. References

Adams, R.H. (2001). Veterinary Pharmacology and Therapeutics. Ames, Iowa, Blackwell Publishing Professional.

Anonym (2009). "Rechstvorschriften zur Frühferkelkastration männlicher Ferkel durch die Tierhalterin oder den Tieralter." Gesetzliche Grundlagen: Tierschutzgesetz (TschG), Tierschutzverordnung (TSchV), Verordnung des EDV über die Ausbildung in der Tierhaltung und im Umgang mit Tieren (AusbildungsV), Heilmittelgesetz (HMG), Verordnung über die Tierarzneimittel (TAMV). BVET. Bern. Art. 16 TSchG, Art. 32 TSchV.

Axiak, S.M. (2007). "Anaesthesia for castration of piglets: comparison of intranasal versus intramuscular ketamine, climazolam and azaperone." Department of Clinical Veterinary Medicine, University of Berne, Division of Anaesthesiology and Division of Clinical Veterinary Research. Dissertation, Vetsuisse Faculty of Berne.

Barash, P.G., Cullen, B.F., Stoelting, R.K. and Cahalan, M.K. (2009). Clinical Anesthesia, Lippincott Williams & Wilkins, a Wolters Kluwer Business.

Baumgartner, J., Laister, S., Koller, M., Pfützner, A., Grodzycki, M., Andrews, S. and Schmoll, F. (2010). "The behaviour of male fattening pigs following either surgical castration or vaccination with a GnRF vaccine." Applied Animal Behaviour Science **124**(1): 28-34.

Bonneau, M., Le Denmat, M., Vaudelet, J.C., Veloso-Nunes, J.R., Mortensen, A.B. and Mortensen, H.P. (1992). "Contributions of fat androstenone and skatole to boar taint: I. Sensory attributes of fat and pork meat." Livestock Production Science **32**: 63-80.

Boschert, K., Flecknell, P.A., Fosse, R.T., Framstad, T., Sjostrand, U., Stevens, J. and Thurmon, J. (1996). "Ketamine and its use in the pig. Recommendations of the Consensus Meeting on Ketamine Anaesthesia in Pigs, Bergen 1994." Laboratory Animals **30**: 209-219.

Burren, N., Jäggin, N. and Schatzmann, U. (2008). "Die Ferkelkastration unter Injektionsnarkose. Weiterführende Unteruchungen." Bericht Projekt ProSchwein. Zollikofen, Schweizerische Hochschule für Landwirtschaft SHL. Departement für klinische Veterinärmedizin, Universität Bern.

Busch, U., Schmid, J., Heinzel, G., Schmaus, H., Baierl, J., Huber, C. and Roth, W. (1998). "Pharmacokinetics of meloxicam in animals and the relevance to humans." Drug Metabolism and Disposition **26**(6): 576-584.

Calvey, T.N. (1995). "Isomerism and anaesthetic drug." Acta Anaesthesiologica Scandinavica **106**: 83-90.

Canet, J. and Castillo, J. (2012). "Ketamine A familiar drug we trust." American Society of Anesthesiologist **116** (1): 6-8.

Clutton, R.E., Blissitt, K.J., Bradley, A.A. and Camburn, M.A. (1997). "Comparison of three injectable anaesthetic techniques in pigs." Veterinary Record **141**: 140-146.

Cornick-Seahorn, J.L. (2001). Veterinary Anesthesia. Woburn, MA 01801-2041, Butterworth-Heinmann, a member of Reed Elsevier group.

De Roest, K., Montanari, C., Fowler, T. and Baltussen, W. (2009). "Resource efficiency and economic implications of alternatives to surgical castration without anaesthesia." Animal **3**(11): 1522-1531.

Deleforge, J., Davot, J., Boisrame, B. and Delatour, P. (1991). "Enantioselectivity in the anaesthetic effect of ketamine in dogs." Journal of Veterinary Pharmacology and Therapeutics **14**: 418- 420.

Duque, J.C., Oleskovicz, N., Guirro, E.C.B.P., Valadão, C.a.A. and Soares, V.E. (2008). "Relative potency of ketamine and S(+)-Ketamine in dogs." Journal of Veterinary Pharmacology and Therapeutics **31**(4): 344-348.

Erhardt, W., Wohlrab, S., Kilic, N., Werner, C. and Henke, J. (2001). "Comparison of the anaesthesia combinations racemic-ketamine/medetomidine and S-ketamine/medetomidine in syrian golden hamsters (mesocricetus auratus)." Veterinary Anaesthesia and Analgesia **28**(4): 212-213.

Fosse, T.K., Haga, H.A., Hormazabal, V., Haugejorden, G., Horsberg, T.E. and Ranheim, B. (2008). "Pharmacokinetics and pharmacodynamics of meloxicam in piglets." Journal of Veterinary Pharmacology and Therapeutics **31**(3): 246-252.

Fredriksen, B., Font I Furnols, M., Lundström, K., Migdal, W., Prunier, A., Tuyttens, F.A.M., Bonneau, M. (2009). "Practice on castration of piglets in Europe." Animal **3**(11): 1480-1487.

Fredriksen, B. and Nafstad, O. (2006). "Surveyed attitudes, perceptions and practices in Norway regarding the use of local anaesthesia in piglet castration." Research in Veterinary Science **81**(2): 293-295.

Ganter, M., Ruppert, K. and Kanngiesser, M. (1990). "The development of a residue-poor anesthesia in swine." Berliner und Münchener Tierärztliche Wochenschrift **103**: 341-348.

Gerritzen, M.A., Kluivers-Poodt, M., Reimert, H.G.M., Hindle, V. and Lambooij, E. (2008). "Castration of piglets under CO_2-gas anaesthesia." Animal **2**(11): 1666-1673.

Gonyou, H., Parfet, K., Anderson, D. and Olson, R. (1988). "Effects of amperozide and azaperone on aggression and productivity of growing-finishing pigs." Journal of Animal Science **66** (11): 2856-2864.

Haga, H.A. and Ranheim, B. (2005). "Castration of piglets: the analgesic effects of intratesticular and intrafunicular lidocaine injection." Veterinary Anaesthesia and Analgesia **32**(1): 1-9.

Hansson, M., Lundeheim, N., Nyman, G. and Johansson, G. (2011). "Effect of local anaesthesia and/or analgesia on pain responses induced by piglet castration." Acta Veterinaria Scandinavia **53**(34).

Heid, A. and Hamm, U. (2009). "Alternativen zur betäubungslosen Ferkelkastration." Fleischwirtschaft **12**: 93-98.

Heinonen, M.L., Raekallio, M.R., Oliviero, C., Ahokas, S. and Peltoniemi, O.A. (2009). "Comparison of azaperone-detomidine-butorphanol-ketamine and azaperone-tiletamine-zolazepam for anaesthesia in piglets." Veterinary Anaesthesia and Analgesia **36**: 151-157.

Heinritzi, K. and König, H. (1988). "Anesthesia in swine." Tierärztliche Praxis **16**(1): 45-52.

Himmelseher, S. and Pfenninger, E. (1998). "The clinical use of S-(+)- ketamine - a determination of its place." AINS - Anästhesiologie Intensivmedizin Notfallmedizin Schmerztherapie **33**(12): 764-770.

Jäggin, N. and Bettschart, R. (2008). “Technische Anforderungen an Geräte für die Inhalationsanästhesie zur Schmerzausschaltung bei der chirurgischen Kastration von Ferkeln.” Zollikofen, Schweizerische Hochschule für Landwirtschaft SHL.

Jäggin, N. and Burren, C. (2008). “Beurteilung von Geräten für die Inhalationsanästhesie zur Schmerzausschaltung bei der chirurgischen Kastration von Ferkeln - Resultate Feldversuche Gerät Pigsleeper, Firma Schippers.” Zollikofen, Schweizerische Hochschule für Landwirtschaft SHL.

Jäggin, N. and Burren, C. (2009). “Beurteilung von Geräten für die inhalationsanästhesie zur Schmerzausschaltung bei der chirurgischen Kastration von Ferkeln - Resultate Feldversuche Gerät PorcAnest, Firma Provet.” Zollikofen, Schweizerische Hochschule für Landwirtschaft SHL.

Jäggin, N., Kupper, T. and Huber-Eicher, B. (2008). “Bewertung der Lokalanästhesie zur Schmerzausschaltung bei der chirurgischen Kastration von Ferkeln.” Zollikofen, Schweizerische Hochschule für Landwirtschaft SHL. Departement für klinische Veterinärmedizin, Universität Bern.

Jud, R., Picek, S., Makara, M.A., Steininger, K., Hässig, M. and Bettschart-Wolfensberger, R. (2010). "Comparison of racemic ketamine and S-ketamine as

agents for the induction of anaesthesia in goats." Veterinary Anaesthesia and Analgesia **37**(6): 511-518.

Keita, A., Pagot, E., Prunier, A. and Guidarini, C. (2010). "Pre-emptive meloxicam for postoperative analgesia in piglets undergoing surgical castration." Veterinary Anaesthesia and Analgesia **37**(4): 367-374.

Kohler, I., Moens, Y., Busato, A., Blum, J. and Schatzmann, U. (1998). "Inhalation Anaesthesia for castration of piglets: CO_2 compared to halothan." Journal of Veterinary Medicine Series A **45**: 625-633.

Kohrs, R. and Durieux, M.E. (1998). "Ketamine: Teaching an Old Drug New Tricks." Anesthesia & Analgesia **87**: 1186-1193.

Koinig, H. and Marhofer, P. (2003). "S(+)-ketamine in paediatric anaesthesia." Pediatric Anesthesia **13**(3): 185-187.

Körtel, A. (1996). "Blutspiegel von Cortisol und Pterinen im Verlauf von Ferkelkastrationen mit und ohne CO_2/O_2-Anästhesie." Dissertation, Veterinärmedizin München.

Kupper, T., Pauly, C., Burren, C., Hofer, A. and Spring, P. (2008). "Alternative Methoden zur konventionellen Ferkelkastration ohne Schmerzausschaltung." Projekt Pro Schwein Schlussbericht 2008. Schweizerische Hochschule für Landwirtschaft SHL, Zollikofen. SUISAG, Sempach.

Lahrmann, K.H. (2006). "Klinisch-experimentelle Untersuchungen zur Ketamine/Azaperon-Allgemeinanästhesie beim Schwein." Praktischer Tierarzt **87**(9): 713-725.

Lahrmann, K.H., Kmiec, M. and Stecher, R. (2005). "Die Saugferkelkastration mit der Ketamin/Azaperon-Allgemeinanästhesie: tierschutzkonform, praktikabel, aber wirtschaftlich?" Praktischer Tierarzt **87**(10): 802-809.

Langhoff, R., Zols, S., Barz, A., Palzer, A., Ritzmann, M. and Heinritzi, K. (2009). "Investigation about the use of analgesics for the reduction of castration-induced pain in suckling piglets." Berliner und Münchner Tierärztliche Wochenschrift **122**: 325-332.

Larenza, M.P., Althaus, H., Conrot, A., Balmer, C., Schatzmann, U. and Bettschart-Wolfensberger, R. (2008a). "Anaesthesia recovery quality after racemic ketamine or S-ketamine adminstration to male cats undergoing neutering surgery." Schweizer Archiv für Tierheilkunde **150**(12): 599-607

Larenza, M.P., Knobloch, M., Landoni, M.F., Levionnois, O.L., Kronen, P.W., Theurillat, R., Schatzmann, U. and Thormann, W. (2008b). "Stereoselective pharmacokinetics of ketamine and norketamine after racemic ketamine or S-ketamine administration in Shetland ponies sedated with xylazine." Veterinary Journal **177**(3): 432-435.

Larenza, M.P., Peterbauer, C., Landoni, M.F., Levionnois, O.L., Schatzmann, U., Spadavecchia, C. and Thormann, W. (2009a). "Stereoselective pharmacokinetics of ketamine and norketamine after constant rate infusion of a subanesthetic dose of racemic ketamine or S-ketamine in Shetland ponies." American Journal of Veterinary Research **70**(7): 831-839.

Larenza, M.P., S.K., R., Kutter, A.P., Conrot, A., Theurillat, R., Kummer, M. and Thormann, W. (2009b). "Evaluation of anesthesia recovery quality after low-dose racemic or S-ketamine infusion during anesthesia with isoflurane in horses." American Journal of Veterinary Research **70**(6): 710-718.

Lauer, S., Zanella, A., Körtel, A., Henke, J. and Scarvogel, S. (1994). "Die CO_2 /O_2-Anästhesie zur Kastration von männlichen Ferkeln." Deutsche Tierärztliche Wochenschrift **101**: 110-113.

Leidig, M.S., Hertrampf, B., Failing, K., Schumann, A. and Reiner, G. (2009). "Pain and discomfort in male piglets during surgical castration with and without local anaesthesia as determined by vocalisation and defence behaviour." Applied Animal Behaviour Science **116**(2): 174-178.

Löscher, W., Ungemach, F.R. and Kroker, R. (2006). Pharmakotherapie bei Haus- und Nutztieren, Georg Thieme Verlag.

Marx, G., Horn, T., Thielebein, J., Knubel, B. and Von Borell, E. (2003). "Analysis of pain-related vocalization in young pigs." Journal of Sound and Vibration **266**(3): 687-698.

McGlone, J.J. and Hellman, J.M. (1988). "Local and general anesthetic effects on behavior and performance of two- and seven-week-old castrated and uncastrated piglets." Journal of Animal Science **66**(12): 3049-3058.

McGlone, J.J., Nicholson, R.I., Hellman, J.M., Herzog, D.N. (1993). "The development of pain in young pigs associated with castration and attempts to prevent castration-induced behavioral changes." Journal of Animal Science **71**: 1441-1446.

Mersmann, H.J. (1989). "Influence of Infused β-Adrenergic Agonists on Porcine Blood Metabolites and Catecholamines." Journal of Animal Science **67**(10): 2633-2645.

Moon, P.F. and Smith, L.J. (1996). "General anesthetic techniques in swine." Veterinary Clinics of North America, Food Animal Practice **12**(3): 663-691.

Morgan, C.J.A. and Curran, H.V. (2011). "Ketamine use: a review." Addiction **107**(1): 27-38

Nishimura, R., Kim, H., Matsunaga, S., Hayashi, K., Tamura, H., Sasaki, N. and Takeuchi, A. (1993). "Comparison of Sedative and Analgesic/Anesthetic Effects

Induced by Medetomidine, Acepromazine, Azaperone, Droperidol and Midazolam in Laboratory Pigs." Journal of Veterinary Medical Science **55**(4): 687-690.

Nishimura, R., Sakaguchi, M., Mochizuki, M., Sasaki, N., Takahashi, H., Tamura, H. and Takeuchi, A. (1992). "A balanced anesthesia with a combination of xylazine, ketamine and butorphanol and its antagonism by yohimbine in pigs." Journal of Veterinary Medical Science **54**(4): 615-620.

Nussbaumer, I., Indermühle, N., Zimmermann, W. and Leist, Y. (2011). "Ferkelkastration mittels Injektionsnarkose: Erfahrungen mit der Kombination Azaperon, Butorphanol und Ketamin." Schweizer Archiv für Tierheilkunde **153**(1): 33-35.

Nussbaumer, I., Zimmermann, W. and Peterbauer, C. (2008). "Anaesthesia of pigs with a combination of romifidine, butorphanol and ketamine." Veterinary Record **163**(24): 720-721.

Plumb, D.C. (2002). Veterinary Drug Handbook, Iowa State Press, Blackwell Publishing Company.

Prunier, A., Bonneau, M., Von Borrel, E.H., Cinotti, S., Fredriksen, B., Giersing, M., Morton, D.B., Tuyttens, F.a.M. and Velarde, A. (2006). "A review of the welfare consequences of surgical castration in piglets and the evaluation of non-surgical methods." Animal Welfare **15**(3): 277-189.

Prunier, A., Mounier, A.M. and Hay, M. (2005). "Effects of castration, tooth resection or tail docking on plasma metabolites and stress hormones in young pigs." Journal of Animal Science **83**: 216-222.

Reich, D.L. and Silvay, G. (1989). "Ketamine: an update on the first twenty-five years of clinical experience." Canadian Journal of Anaesthesia **36**(2): 186-197.

Sakaguchi, M., Nishimura, R., Sasaki, N., Ishiguro, T., Tamura, H. and Takeuchi, A. (1992). "Enhancing effect of butorphanol on medetomidine-induced sedation in pigs." Journal of Veterinary Medical Science **54**(6): 1183-1185.

Sakaguchi, M., Nishimura, R., Sasaki, N., Ishiguro, T., Tamura, H. and Takeuchi, A. (1996). "Anesthesia induced in pigs by use of a combination of medetomidine, butorphanol, and ketamine and its reversal by administration of atipamezole." American Journal of Veterinary Research **57**(4): 529-534.

Schmidt, A., Øye, E. and J., A. (2005). "Cerebral physiological responses to bolus injection of racemic, S(+)- or R(-)-ketamine in the pig." Acta Anaesthesiologica Scandinavica **49**(10): 1436-1442.

Schulz, C. (2007). "Auswirkung einer Isofluran-Inhalationsnarkose auf den Kastrationsstress und die postoperativen Kastrationsschmerzen von Ferkeln." Klinik für Schweine. Dissertation, Ludwig-Maximilians-Universität München.

Schüttler, J. and Schwilden, H. (2008). Modern Anesthetics. Berlin-Heidelberg, Springer-Verlag.

Symoens, J. (1970). "Prevention and treatment of aggression and stress in pigs by means of the neuroleptic azaperone." Deutsche Tierärztliche Wochenschrift **77**(6): 144-148.

Symoens, J. and Van Den Brande, M. (1969). "Prevention and cure of aggressiveness in pigs using the sedative azaperone." Veterinary Record **85**(3): 64-67.

Von Borell, E., Baumgartner, J., Giersing, M., Jäggin, N., Prunier, A., Tuyttens, F.a.M. and Edwards, S.A. (2009). "Animal welfare implications of surgical castration and its alternatives in pigs." Animal **3**(11): 1488-1496.

White, P.F., Schüttler, J., Shafer, A., Stanski, D.R., Horai, Y. and Trevor, A.J. (1985). "Comparative pharmacology of the ketmamine isomers. Studies in volunteers." British Journal of Anaesthesia **57**(2): 197-203.

Zols, S., Ritzmann, M. and Heinritzi, K. (2006). "Effect of a local anaesthesia in castration of piglets." Tierärztliche Praxis Grosstiere **34**(2): 103-106.

9. Acknowledgements

For supervising the project and for every advice I needed, I would like to thank Prof. Dr. med. vet, PhD. Regula Bettschart-Wolfensberger. Thank you for the opportunity to realise this project and the thesis.

A big thank you to everyone who helped hands-on at the farm on the trial day. It would not have been possible without you all: Sara Furrer, Anja Lippuner, Martin Handke, Max Abé, Flurina Koller and Ladina Caviezel.

For letting us realise the trial with their animals on the farm Aemethof, my thanks go to Roland Nussbaumer and Martin Hächler and their families.

With the help of Prof. Dr. med. vet. Michael Hässig the statistical evaluations were carried out successfully. Thank you for your enormous patience.

Thanks to my boyfriend Fabian Zollet who never gave up believing in this thesis and me and has supported me with his constant encouragement and his technical computer knowledge. Thank you for proofreading the thesis as well and your patience with me.

My thanks go to my family who helped me through the time of my studies and thesis and especially to my dad David Stauffer for reviewing my spelling mistakes.

10. Curriculum Vitae

Persönliche Angaben

Name	Stauffer, Stephanie Rebecca
Geburtsdatum	12.03.1984
Geburtsort	Lenzburg AG
Nationalität	Schweizerin/Spanierin
Heimatort	Hallwil AG

Ausbildung

August 1991 – Juni 2000	Primarschule und Oberstufe Seon
August 2000 – Juni 2004	Matura, Alte Kantonsschule Aarau
Oktober 2005 – Juli 2010	Vetsuisse-Fakultät Universität Bern
August 2010 – Oktober 2012	Dissertation am Departement für Pferde, Abteilung für Anästhesiologie (Prof. Dr. med. vet. PhD Regula Bettschart-Wolfensberger), Vetsuisse-Fakultät Universität Zürich

Anstellungen

August 2010 – Oktober 2010	Dissertation, Departement für Pferde, Abteilung für Anästhesiologie, Vetsuisse-Fakultät Universität Zürich
November 2010 – Mai 2012	Equine Intern, Donnington Grove Veterinary Surgery, Newbury, UK
August 2012	Assistentin, Tierärztliche Gemeinschaftspraxis Zücken AG, Ruswil

11. Annexe

11.1 Scoring and timing sheet

Versuchsnummer: _____ IM-Injektion Uhrzeit: _____

Einschlafen

Timing	Zeit	Nach 15 Min Ja Nein		Besonderes/Beobachtungen
Brustlage				
Seitenlage				
Keine Bewegungen mehr				
Nachdosierung (was/wie viel/warum)				

Score	Torkeln/Ataxie		Ruderbewegung		Repetiertes Aufstehen & Abliegen		Besonderes/ Beobachtungen
0		Keine Ataxie		Keine Ruderbewegungen		Einmaliges Abliegen	
1		2-4 Schritte Ataxie		Einmaliges Rudern		> 1x Aufstehen	
2		> 4 Schritte Ataxie		Repetiertes Rudern		> 3x Aufstehen	
3		> 10 Schritte Ataxie		Kontinuierliches Rudern		> 6x Aufstehen	
Zeit	B	E	B	E	B	E	

Anästhesie/Analgesie/Kastration

Timing	Zeit		Besonderes/ Beobachtungen
A: vor Kastration			Berührung, Kneifen in Nasenseptum
B: Verbringen in Kastrationsposition			
C1: 1.Schnitt / C2: 2.Schnitt			Beginn Kastration
D1: 1.Samenstrang abklemmen / D2: 2.S.a			
Webringen aus Kastrationsposition			Ende Kastration
Nachdosierung (was/wie viel)			

Score	A	B	C	D	Anzahl Bewegungen	A	B	C	D	Intensität Bewegung	A	B	C	D	Vokalisation	Besonderes/ Beobachtungen
0					Keine Bewegung					Keine Bewegung					Keine Vokalisation	
1					Einmalige Bewegung					Bewegen einer Gliedmasse					Einmalige Vokalisation	
2					Repetiertes Bewegen					Bewegen von mehr als einer Gliedmasse					Repetierte Vokalisation	
3					Kontinuierl. Bewegen					Inklusive Wirbelsäule					Kontinuierliche Vokalisation	
4										Wie 3, stärke Reaktion						

Aufwachen

Score	Ruderbewegungen		Krämpfe		Aufstehversuche	
0		Keine Ruderbewegung		Kein Krampf		Einmaliges Aufstehen
1		Einmaliges Rudern		Einmaliger Krampf		> 1 Versuch
2		Repetiertes Rudern		Repetierte Krämpfe		> 3 Versuche
3		Kontinuierliches Rudern		Kontinuierliche Krämpfe		> 6 Versuche
Zeit	B	E	B	E	B	E

Besonderes/ Beobachtungen

11.2 Table medication

Medikamente 08.09.2010

Substanz	Medikament	Konzentration	Dosierung/ Tier	Dosis in ml pro kg	Dosis in ml pro Ferkel à 25kg	½ Dosis	¼ Dosis
Azaperon	Stresnil, Biokema SA	40 mg/ml	5 mg/kg	0.125 ml	3.125 ml	1.55 ml	
Butorphanol	Morphasol 10-, Dr. E. Gräub AG	10 mg/ml	0.2 mg/kg	0.02 ml	0.5 ml		
Ketamin Racemat	Ketasol-100, Dr E. Gräub AG	100 mg/ml	15 mg/kg	0.15 ml	3.75 ml	1.875 ml	0.9375 ml
S-Ketamin	Keta- S, Dr. E. Gräub AG	60 mg/ml	9 mg/kg	0.15 ml	3.75 ml	1.875 ml	0.9375 ml
Meloxicam	Metacam 20, Boehringer Ingelheim	20 mg/ml	0.4 mg/kg	0.02 ml	0.5 ml		
Lidocain	Lidocain HCl 2%, Kantonsapotheke Zürich	20 mg/ml			2.5ml pro Samenstrang, 5ml total		

Totale Dosis für ein Tier vom Gemisch: 0.295 ml/KGW IM → 7.375 ml/ 25 kg Ferkel

Nachdosierung mit Ketasol-100 oder Keta S je nach Gruppenzugehörigkeit: ½ Dosis oder ¼ Dosis iv.
Tabelle anhand von Narkosetabelle von Y. Leist und I. Nussbaumer und Clinipharm erstellt

11.3 Liste with groupe allocation and eartag number

Liste

Nummer	OM-Nummer	A	B
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			
14			
15			
16			
17			
18			
19			
20			
21			
22			
23			
24			
25			
26			
27			
28			

11.4 Table timing recovery and bodyweight

Timing Aufwachen

Zeit	Erste Bewegungen	Brustlage	Stehfähig	KGW
1				
2				
3				
4				
5				
6				
7				
8				
9				
19				
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				
21				
22				
23				
24				
25				
26				
27				
28				
29				
30				
31				
32				
33				
34				
35				
36				
37				
38				
39				
40				